

AD _____

MIPR NO: 92MM2525

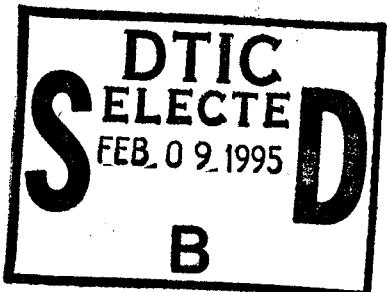
TITLE: SUBCHRONIC TOXICITY STUDIES ON 1,3,5-TRINITROBENZENE,
1,3-DINITROBENZENE, AND TETRYL IN RATS

SUBTITLE: Subchronic Toxicity Evaluation of N-Methyl-N,
2,4,6-Tetranitroaniline (Tetryl) in Fischer 344 Rats

PRINCIPAL INVESTIGATOR: Tirumuru V. Reddy, Ph.D.

CONTRACTING

ORGANIZATION: Environmental Monitoring Systems Laboratory
U.S. Environmental Protection Agency
26 W. Martin Luther King Drive
Cincinnati, Ohio 45268-0001



REPORT DATE: September 1, 1994

19950206 013

TYPE OF REPORT: Final Report

PREPARED FOR: U.S. Army Medical Research and Materiel Command,
Fort Detrick, Frederick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for public release;
distribution unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE

Form Approved

OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY (Leave blank)			2. REPORT DATE 1 September 1994		3. REPORT TYPE AND DATES COVERED Final Report		
4. TITLE AND SUBTITLE Subchronic Toxicity Studies on 1,3,5-Trinitrobenzene, 1,3-Dinitrobenzene, and Tetryl in Rats SUBTITLE: Subchronic Toxicity Evaluation of N-Methyl-N, 2,4,6-Tetranitroaniline (Tetryl) in Fischer 344 Rats			5. FUNDING NUMBERS MIPR No. 92MM2525				
6. AUTHOR(S) Tirumuru V. Reddy, F. B. Daniel, M. Robinson, G. R. Olson, B. Wiechman, G. Reddy							
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Environmental Monitoring Systems Laboratory U.S. Environmental Protection Agency 26 W. Martin Luther King Drive Cincinnati, Ohio 45268-0001				8. PERFORMING ORGANIZATION REPORT NUMBER			
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command, Fort Detrick Frederick, Maryland 21702-5012				10. SPONSORING / MONITORING AGENCY REPORT NUMBER			
11. SUPPLEMENTARY NOTES							
12a. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited				12b. DISTRIBUTION CODE			
13. ABSTRACT (Maximum 200 words) Subchronic toxic effects of N-Methyl-N, 2,4,6-Tetranitroaniline (tetryl) in male and female Fisher 344 rats were evaluated by feeding powdered certified laboratory chow supplemented with varied concentrations of tetryl (0, 200, 1000 and 3000 mg/kg diet) for ninety days. There were no clinical signs of toxicity or early deaths. Food intake was reduced in both sexes at all dose levels throughout the study and resulted in a significant decrease in terminal body weights in the 3000 and 1000 mg tetryl dose groups. The calculated average tetryl dosage was 14, 69 and 199 mg/kg/day for females and 13, 62 and 180 mg/kg/day for males. An increase in the relative liver and kidney weights in both sexes in the 3000 and 1000 mg tetryl dose groups and an increase in the relative spleen weight in the 3000 mg dose group were noted. Hematology and clinical chemistry analyses were done at 45 and 90 days exposure. Methemoglobin levels were increased in both sexes in the 3000 and 1000 tetryl dose groups at 45 and 90 days while hemoglobin was decreased in these same groups at 90 days. The red blood cell count was decreased in the 3000 mg tetryl dose group of both sexes while the reticulocyte count was increased in this same group. Cholesterol levels were increased in all dose groups in both sexes at 90 days. Histopathological examinations suggested that susceptible organs for tetryl toxicity were spleen (pigment deposition and erythroid cell hyperplasia) and kidneys (tubular degeneration and cytoplasmic droplets). A no observed adverse effect level (NOAEL) of 13 mg/kg/day was established.							
14. SUBJECT TERMS Subchronic Oral Toxicity Fischer 344 Rats Hematology			Methemoglobin Tetryl 90-Day Clinical Chemistry N-Methyl-N, 2,4,6-Tetranitroaniline		15. NUMBER OF PAGES 16. PRICE CODE		
17. SECURITY CLASSIFICATION OF REPORT Unclassified		18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified		19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified		20. LIMITATION OF ABSTRACT Unlimited	

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)

Prescribed by ANSI Std. Z39-18

298-102

DTIC QUALITY INSPECTED

QUALITY ASSURANCE STATEMENT

The portions of this toxicology project performed and reported by Pathology Associates, Inc. has been inspected and audited by the quality assurance unit as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Environmental Protection Agency. The following table is a record of the inspections/audits performed and reported by the QAU.

<u>Date of Inspection</u>	<u>Phase Inspected</u>	<u>Date Findings Reported to Management and Study Director</u>
01-03-95	Final Report	01-03-95
08-29-94	Draft Report	08-29-94
08-29-94	Data	08-29-94
04-14-94	Necropsy	04-14-94
04-08-94	In-Life Data	04-12-94
04-08-94	Food & Water Consumption	04-12-94
02-15-94	Food & Water Consumption	02-17-94
02-15-94	Weighing	02-17-94
01-13-94	Food & Water Consumption	01-14-94
01-13-94	Weighing	01-14-94


Wilma Fox, MA
Quality Assurance Unit
PAI-Cin

1-3-95
Date

Study Number: 94-001

Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
By	
Distribution	
Availability Codes	
Dist	Avail and/or Special
A-1	

Compliance Statement

This study was conducted in compliance with the Good Laboratory Practice Regulations as set forth in Title 21 of the U.S. Code of Federal Regulations Part 792 issued August 17, 1989. All deviations from the protocol and/or GLPs are listed in Appendix J. There were no deviations from the aforementioned regulations which affected the quality or integrity of the study or the interpretation of the results in the report.

Tirumuru V. Reddy

Tirumuru V. Reddy, Ph.D.
U.S. Environmental Protection Agency

12-30-94

Date

Greg R. Olson

Greg R. Olson, D.V.M., Ph.D.
Pathology Associates, Inc.

12/30/94

Date

Joni A. Torsella

Joni A. Torsella, Ph.D.
U.S. Environmental Protection Agency

12/30/94

Date

Barry E. Wiechman

Barry E. Wiechman, B.S., M.S.
Pathology Associates, Inc.

12-29-94

Date

Study Personnel

Principal Investigator: Tirumuru V. Reddy, Ph.D.

Co-Principal Investigator: F.Bernard Daniel, Ph.D.

Biochemist: Barry E. Wiechman, B.S., M.S.

Pathologist: Greg R. Olson, D.V.M., Ph.D.

Biostatistician: Joni A. Torsella, Ph.D.

Study Biological Technician: Bradley Peterson, A.S.

Histology Laboratory Supervisor: Sheree Lovelace, A.S.

Contracting Officer Representative: Gunda Reddy, Ph.D.

Study Timetable:

Study Initiation: January 4, 1994

Initiation of Dosing: January 12, 1994

Completion of Necropsy: April 14, 1994

TABLE OF CONTENTS

	Page Number
Introduction	1
Materials and Methods	2
Results	5
Summary	9
References	10
Tables	11
Appendices	
A. Food and Water Consumption Data	25
B. Body Weights	40
C. Organ Weights	45
D. Hematology Data	55
E. Clinical Chemistry Data	64
F. Clinical Observations	73
G. Gross and Histopathology Data	77
H. Ophthalmology Data	124
I. Chemical Analyses	127
J. Protocol and Amendments Deviations from GLP's and Protocol	138

INTRODUCTION

Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. TNB is formed during the nitration step of TNT synthesis as a result of oxidation of methyl groups. Although the complete mechanism of TNB formation during TNT photolysis is unknown, it has been suggested that it is produced by decarboxylation of 2,4,6-trinitrobenzaldehyde, a major TNT photoproduct (Burlinson, 1980). It is also found in aquatic systems and surface soils as a by-product of photolysis of TNT. DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out, and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of these compounds (Walsh and Jenkins, 1992).

Toxicity data on these compounds are limited. The oral LD₅₀ of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD₅₀ of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits were noted. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs (Fitzgerald et. al., 1992 a,b,c). Some of the toxicological effects of DNB are: formation of methemoglobin, testicular degeneration and reproductive failure, weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin (Von Burg, 1989). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Dermatitis, liver atrophy, spleen effects, headaches, weight loss and respiratory irritation were reported following tetryl exposure (U.S. EPA, 1990). Atmospheric concentration of 1.5 mg/m³ or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB, and tetryl have been shown to be genotoxic in the Salmonella mutagenesis assay (McGregor et. al., 1989). TNB has also been shown to form adducts of blood proteins and tissue DNA in rats (Reddy et. al., 1991).

Objective of the Study

This study was conducted in order to evaluate the toxicity of tetryl when administered in the diet for 90 days.

MATERIALS AND METHODS

Test Material Preparation

N-Methyl-N, 2,4,6-Tetranitroaniline powder (CAS #479-45-8) 99.45% purity was prepared by Dr. W. Koppes of the Naval Surface Warfare Center. The purity was confirmed by the U.S. Army Biomedical Research and Development Laboratory and the U.S. EPA. Analysis by HPLC revealed no detectable impurities. Certified powdered Purina Laboratory Chow 5002 was purchased (Ralston-Purina Co., St. Louis, MO) and stored at 4°C until used. Tetryl diets were prepared weekly. First, 4.5 g of tetryl was added to 50 g of powdered diet in a mortar and thoroughly ground with a pestle. Afterwards 1450 g of the diet was added and mixed for 2 hours in a mechanical mixer (Kitchen Aid, St. Joseph, MI)) for uniform distribution. This was verified by determining the tetryl concentration in the diet, taken from each of the 1 kg mixtures, by quantitative analysis done by HPLC. The premixed diet was further diluted with fresh powdered diet to obtain the desired tetryl concentration in the lower dose groups. The diet feeders were refilled twice a week and changed weekly.

Analyses of the tetryl-feed mixtures were carried out on acetone extracts of the mixtures, utilizing a Waters 600E chromatography system (Waters, Milford, MA), equipped with a 490E programmable multiwavelength detector, operating at 245 nm. The entire chromatography system was interfaced with a Berthold HPLC computer program, Version 1.65 (Berthold, Nashua, NH). The tetryl was eluted from a Zorbax C-8 column (9.4 mm x 25 cm) (MAC-DOD Analytical, Chadds Ford, PA) with a water-methanol gradient, at a flow rate of 3 ml/min. The gradient had an initial condition of 20% methanol which was increased in a linear fashion from 20% to 50% in 15 minutes and then to 65% in 25 minutes, and finally to 100% in 10 minutes. The column was washed for an additional 5 minutes and brought back to 20% methanol by reverse gradient and equilibrated for an additional 10 minutes at initial conditions before the next sample was injected. Working standards were prepared in Burdick and Jackson HPLC grade high purity methanol (Baxter, Obetz, OH). Analytical data of these mixtures is presented in Appendix I.

Animals and Maintenance

Male and female Fischer 344 rats, confirmed free of viral antibodies, bacteria and parasites, were obtained from Charles River Laboratories, Kingston, New York. The animals, 6-7 weeks old and weighing approximately 125 g when delivered, were held for 1 week in quarantine prior to initiation of treatment. The animals were housed in a temperature (20-22°C) and humidity (40-60%) controlled room on a 12:12 hour light:dark cycle. For the study, they were housed individually in polycarbonate cages and water was administered ad libitum. Animal identification was done using electronic implants (Bio Medic, Maywood, NJ) with the rats assigned to control and treatment groups according to a computer-generated set of random numbers. The weight variation of the animals of each sex used did not exceed \pm 2 s.d. of the mean weight at the time of delivery. The cages were identified with a color-coded identification card indicating the animal and treatment

group. All aspects of the study were conducted in compliance with the guidelines of the American Association for Accreditation of Laboratory Animal Care.

All rats were observed twice daily for physiological and behavioral responses as well as for mortality or morbidity. Food and water consumption were recorded twice weekly. Body weights were taken prior to the start of the study, once weekly during the study and at the final sacrifice.

Experiment Design

Group	No. of Animals	Sex	Dose Groups (mg tetryl/kg diet)
1	10	F	3000
2	10	F	1000
3	10	F	200
4	10	F	0
5	10	M	3000
6	10	M	1000
7	10	M	200
8	10	M	0

Hematology and Clinical Chemistry

Hematology and clinical chemistry analyses were done on days 45 and 90. Hematology parameters were assessed using a Serono-Baker Hematology Analyzer, Model 9000, coupled to a computer running Labcat® software (Innovation Programming, Inc., Princeton, NJ). Total red and white blood cell counts, platelet count, differential leukocyte count, hemoglobin, and packed cell volume were measured and computed. Methemoglobin samples were analyzed on a IL 482 Co-Oximeter. Heinz bodies were determined using the crystal violet procedure (Lee et. al., 1993) with microscopic examination for positive cells (>5 Heinz bodies).

Clinical chemistry was performed using a Cobas Fara II centrifugal analyzer (Roche, Nutley, NJ) with a non-selective electrode (ISE) module. This system was also interfaced with a personal computer and the Labcat software system. Clinical chemistry analytes included sodium, potassium, total protein, albumin, calcium, phosphorus, total bilirubin, blood urea nitrogen, creatinine, alanine aminotransferase, aspartate aminotransferase, glucose, cholesterol, triglycerides and alkaline phosphatase.

Statistical Evaluation

Males and females were considered separately in all statistical analyses. A one-factor (dose) analysis of variance (ANOVA) was used to analyze normally-distributed measures: body weights, organ weights, organ weight ratios, food and water consumption, hematology and clinical chemistry. When a treatment effect was noted ($p \leq 0.05$, F-test) the difference between the control and the treatment groups was probed using a multiple comparison procedure (Dunnett's t-test).

Necropsy and Histopathology

Prior to necropsy, the animals were anesthetized with pentobarbital (60 mg/kg b.w., i. p.) and blood samples were collected via cardiac puncture after the body weight was recorded. Following euthanasia via exsanguination, all external surfaces, orifices, external surface of the brain, cervical tissues, all organs, and the thoracic, abdominal and pelvic cavities were examined for gross lesions.

During necropsy the following tissues were weighed: brain, liver, spleen, kidneys, adrenals, lungs, thymus, testes w/epididymides, ovaries, and heart.

The following tissues were harvested from each animal and preserved in 10% neutral buffered formalin:

skin	colon
mandibular and	cecum
mesenteric lymph nodes	rectum
mammary glands	liver
thigh muscle	pancreas
sciatic nerve	spleen
sternum	kidneys
femur with marrow	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs with bronchi	prostate
heart and aorta	testes, including epididymides
thyroid	ovaries
parathyroids	uterus
esophagus	nasal cavity with turbinates
stomach	brain
duodenum	pituitary
jejunum	preputial or clitoral glands
tongue	Zymbal's gland
salivary gland	thoracic spinal cord
ileum	harderian gland
eyes	

Subsequently, these tissues were trimmed, processed and embedded in paraffin. Blocks were sectioned at 5 μ and slides were prepared and stained with hematoxylin and eosin. All tissues were examined in the high dose and control groups of both sexes. The spleen and kidneys were identified as target organs and examined in the appropriate groups.

The inflammatory and degenerative lesions were graded according to severity using a scale of one to four (minimal, mild, moderate or marked). Data were tabulated according to individual animal and summarized by group. In addition, the gross observations and microscopic diagnoses were correlated for each animal. Labcat histopathology software was used for data management.

Specimen, Raw data, and Final Report Storage

All tissue specimens, blocks and slides, raw data and final report will be placed in the U.S. EPA storage facility.

RESULTS

Food and Water Consumption

Overall food and water consumption data are listed in Table 1, while weekly data is given in Appendix A. The food consumption was significantly ($p \leq .05$) reduced in all treatment groups of both sexes while water consumption was increased in the high dose (3000 mg tetryl) female group only.

Using the food consumption data, the average daily tetryl dose levels received by group (see Experimental Design) are presented in Table 2.

Body Weights, Organ Weights and Weight Ratios

The mean group values for body weights are listed in Table 3 while mean group organ weights (heart, brain, spleen, adrenals, thymus, ovaries/testes, kidneys, lungs and liver) are given in Tables 4 (females) and 5 (males). Mean group values for organ to body weight ratios and terminal body weights are present in Tables 6 (females) and 7 (males). Individual body weights are found in Appendix B with individual organ weights present in Appendix C.

Significant ($p \leq 0.05$) decreases in terminal body weights were noted in both sexes receiving 3000 mg/kg tetryl diet and in females receiving 1000 mg/kg.

Absolute and relative organ weights were significantly ($p \leq 0.05$) different from controls for the following organs:

Kidneys - An increased relative weight was noted in all treatment groups of both sexes except the male 200 mg tetryl dose group.

Liver - The 3000 mg tetryl dose group of both sexes had increased absolute and relative weights while the 1000 mg/kg dose group of both sexes had only an increased relative weight.

Spleen - The 3000 mg tetryl dose group of both sexes had an increased relative weight with the male group also having an increased absolute weight.

Brain - The 3000 mg tetryl dose group of both sexes had a decreased absolute weight with the female 1000 mg/kg dose group also being decreased.

Adrenals and Thymus - The female 3000 mg tetryl dose group had a decreased absolute weight for both organs while the 1000 mg/kg female dose group also had a decreased adrenal weight.

Hematology

Hematology analyses performed were total white blood cell count (WBC), platelet count, red blood count (RBC), methemoglobin (MetHb), hemoglobin (HGB), hematocrit (HCT), reticulocytes, Heinz bodies and differential leukocyte count for 45 and 90 days. Group data are summarized in Tables 8-11. Individual data are listed in Appendix D.

1. WBC and Differential:

At 45 days, there were no significant changes while at 90 days the female 200 mg tetryl dose group had a significant ($p \leq 0.05$) decreased WBC value.

2. RBC:

At 45 days, females receiving 3000 mg tetryl had a significant ($p \leq 0.05$) decreased RBC while at 90 days both sexes were decreased in this same dose group.

3. Hemoglobin:

At 45 days, females in the 3000 and 1000 mg tetryl dose groups had significantly ($p \leq 0.05$) decreased hemoglobin values as well as males in the 3000 mg dose group. At 90 days both sexes receiving 3000 and 1000 mg tetryl had decreased values.

4. Hematocrit:

At 45 days, there were no significant changes while at 90 days males receiving 3000 and 1000 mg tetryl had significantly ($p \leq 0.05$) decreased hematocrit values.

5. Platelets:

At 45 days, males in the 3000 and 1000 mg tetryl dose groups had significantly ($p \leq 0.05$) increased platelet levels. At 90 days, females in these same dose groups also had increased values. A similar increase was evident in males receiving 3000 mg tetryl.

6. Reticulocytes:

At 45 and 90 days, both sexes dosed at 3000 mg tetryl had significantly ($p \leq 0.05$) increased reticulocyte values as well as females receiving 1000 mg tetryl for 90 days.

7. Methemoglobin:

At both 45 and 90 days, both sexes receiving 3000 and 1000 mg tetryl had significantly ($p \leq 0.05$) increased methemoglobin levels in addition to the 200 mg female group at 45 days.

8. Heinz Bodies:

Were not detected in any group at either 45 or 90 days.

Clinical Chemistry

The mean group values for each analyte are compiled in Tables 12-15. Individual data are present in Appendix E.

1. Total Protein:

At 45 days, all male groups receiving tetryl had significantly ($p \leq 0.05$) increased levels of total protein while at 90 days both sexes in the 3000 and 1000 mg tetryl groups had increased values.

2. Albumin:

At 45 and 90 days, males receiving 3000 and 1000 mg tetryl had significantly ($p \leq 0.05$) increased values for albumin while all treated female groups at 90 days only were increased.

3. Calcium:

At 45 and 90 days, males receiving 3000 and 1000 mg tetryl had significantly ($p \leq 0.05$) increased calcium levels.

4. Total Bilirubin:

At 45 days, females in the 3000 mg tetryl dose group had a significantly ($p \leq 0.05$) increased total bilirubin value while at 90 days both sexes receiving 3000 and 200 mg tetryl had increased levels in addition to the 1000 mg male group.

5. Blood Urea Nitrogen (BUN):

There were no significant differences amongst the groups at either 45 or 90 days except for a slight increase in the 1000 mg male group at 90 days.

6. Creatinine:

At 45 days, females receiving 3000 and 1000 mg tetryl had significantly ($p \leq 0.05$) increased values while at 90 days no changes were noted amongst any of the groups.

7. Aspartate Aminotransferase (AST):

There were no significant differences amongst the groups at either 45 or 90 days except for a slight increase in the 200 mg female group at 90 days.

8. Alanine Aminotransferase (ALT):

There were no significant differences amongst the groups at either 45 or 90 days.

9. Alkaline Phosphatase (ALK Phos):

At 45 days, there were no significant changes while at 90 days all male groups receiving tetryl and the female high dose group (3000 mg tetryl) had significantly ($p \leq 0.05$) decreased values.

10. Sodium:
There were no significant differences amongst the groups at either 45 or 90 days.
11. Potassium:
At 45 days, the male group receiving 3000 mg tetryl had a significantly ($p \leq 0.05$) increased value while at 90 days none of the groups displayed any changes.
12. Glucose:
There were no significant changes amongst the groups at either 45 or 90 days except for a slight increase in the 1000 mg female group at 90 days.
13. Phosphorus:
There were no significant changes amongst the groups at either 45 or 90 days.
14. Cholesterol:
At 90 days, cholesterol was significantly ($p \leq 0.05$) increased at all dose levels in both sexes.
15. Triglycerides:
At 90 days, females receiving 3000 mg tetryl had a significantly ($p \leq 0.05$) reduced triglyceride level.

Clinical Observations

Clinical observations are listed in Appendix F. There were no clinical observations that were meaningful.

Mortality

There were no early deaths in any of the groups.

Ophthalmology Findings (Appendix H)

All animals used in this study were affected with mild corneal dystrophy prior to the initiation of the study which is a common finding in Fischer 344 rats of both sexes. In the time since performing the initial ophthalmic examination the corneal dystrophy lesions had not progressed except in one animal. The remaining abnormalities were sporadic and did not appear to be a dose-related effect.

Gross Pathology

Gross changes noted at the terminal sacrifice were not remarkable.

Histopathology (Appendix G)

All tissues were histopathologically examined in control and high dose animals. The spleen and kidneys were examined in all remaining groups of both sexes.

The spleen was characterized in both sexes in the 3000 mg tetryl dose group by prominent deposition of intra- and extracellular pigment (probable hemosiderin). Also, males in this same dose group showed excessive erythroid cell hyperplasia.

Pigment deposition was also evident in high and mid dose groups (3000 and 1000 mg tetryl) involving the renal cortical epithelium of both sexes. Kidneys in males were further characterized by a dose related increased severity of tubular degeneration and regeneration, hyaline casts, and cytoplasmic droplets. These droplets were morphologically similar to the hyaline droplets noted in the 14 day tetryl study except for a diminished intensity of eosinophilic staining. The remaining diagnoses as listed in the tables should be considered spontaneous since their incidence or severity levels were low.

SUMMARY

The administration to Fischer 344 rats of N-Methyl-N, 2,4,6-Tetranitroaniline at various doses in the diet for ninety days resulted in the following significant findings:

1. A significant decrease in food consumption in both sexes at all dose levels (3000, 1000 and 200 mg tetryl).
2. Terminal body weights were significantly decreased in both sexes in the 3000 mg tetryl dose group and in the female 1000 mg dose group.
3. Relative organ weights were significantly increased in both sexes in the 3000 and 1000 mg tetryl dose groups for liver and kidneys while the spleen was increased in only the 3000 mg dose group.
4. Methemoglobin levels and reticulocytes were significantly increased in both sexes in the 3000 and 1000 mg tetryl dose groups except in females receiving 1000 mg tetryl (reticulocytes).
5. The red blood cell count was significantly decreased in both sexes in the 3000 tetryl dose group while hemoglobin levels were decreased in both the 3000 and 1000 mg dose groups.
6. Cholesterol was significantly increased in both sexes at all dose levels while alkaline phosphatase was decreased in all male groups and the high dose female group (3000 mg tetryl).
7. Albumin levels were significantly increased in both sexes at all dose levels except the female 200 mg tetryl group while total bilirubin was increased at all dose levels except in the female 1000 mg group.

8. The high dose group (3000 mg tetryl) featured prominent splenic pigment deposition along with erythroid cell hyperplasia while males receiving 3000 and 1000 mg tetryl demonstrated increased renal tubular degeneration and regeneration along with obvious cytoplasmic droplets.
9. A no observed adverse effect level (NOAEL) of 13 mg/kg/day was established even though several analytes (hematological and clinical chemistries) in the 200 mg/kg dose group appeared statistically significant, they were not biologically meaningful since the values were within an accepted normal reference range.

REFERENCES

- Burlinson, N.E. (1980) Fate of TNT in an Aquatic Environment: Photodecomposition vs. Biotransformation. Final report. Silver Spring, Maryland: Naval Weapons Center, NSWC/TR-79-445.
- Fitzgerald, G.B., Austin, A., Desai, L.S. and Reddy, G. (1992a). Acute Toxicological Evaluation of N-Methyl-N, 2,4,6-Tetranitroaniline. J. Amer. Coll., Toxicol. Acute Toxicity Data: Part B. 1, 167-168.
- Fitzgerald, G.B., DiGiulio, N., Desai, L.S. and Reddy, G. (1992b). Acute Toxicological Evaluation of 1,3-Dinitrobenzene. J. Amer. Coll., Toxicol. Acute Toxicity Data: Part B. 1, 168-169.
- Lee, R.G., Bithell, T.C., and Foerster, J. (1993). Wintrobe's Clinical Hematology, p.1048.
- Fitzgerald, G. B., DiGiulio, N., Desai, L. S. and Reddy, G. (1992c). Acute Toxicological Evaluation of 1,3,5-Trinitrobenzene. J. Amer. Coll., Toxicol. Acute Toxicity Data: Part B. 1, 169-170.
- McGregor, D.B., Riach, C.G., Hastwell, R.M. and Dacre, J.C. (1980). Genotoxic Activity in Microorganisms of Tetryl, 1,3-Dinitrobenzene and 1,3,5-Trinitrobenzene. Environ. Mut. 2, 531-541.
- Reddy, T.V., Wan, L., Lin, E.L.C., Daniel, F.B. and Reddy, G. (1991). Formation and Persistence of 1,3,5-Trinitrobenzene Adducts with Blood Proteins and Tissue DNA. Toxicologist, 11, 131.
- U.S. EPA. (1990). Health and Environmental Effects Document for Trinitrophenylmethylnitramine. Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH. ECAO-CIN-GO91.
- Von Burg, R. (1989). Toxicology Update: Dinitrobenzene. J. Appl. Toxicol. 9, 199-202.
- Walsh, M.E. and Jenkins, T.F. (1992). Identification of TNT Transformation Products in Soil. U.S. Army Corps of Engineers, Cold Regions Research and Engineering Laboratory, Special Report 92-16.

Table 1: Food and Water Consumption

Dose Groups (mg tetryl/kg diet)	Food	Water (g/kg b.w./day)
Females		
0	74.39 ± 0.54	109.15 ± 1.77
3000	67.55 ± 0.50*	130.13 ± 4.61*
1000	69.35 ± 0.23*	115.89 ± 2.69
200	72.44 ± 0.65*	111.88 ± 2.00
Males		
0	68.50 ± 0.45	85.84 ± 1.83
3000	60.95 ± 0.29*	92.29 ± 2.34
1000	62.87 ± 0.37*	88.72 ± 1.30
200	66.32 ± 0.42*	89.29 ± 2.22

Mean ± Standard Error

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 2: Daily Consumption of Tetryl

Dose Groups (mg/kg diet)	Target Dose (mg/kg b.w.)	Females (mg/kg b.w.)	Males (mg/kg b.w.)
0	0		
3000	300	199.06 ± 1.48	179.63 ± 0.86
1000	100	68.87 ± 0.23	62.43 ± 0.37
200	20	14.20 ± 0.13	13.00 ± 0.08

Mean ± Standard Error

Table 3: Body Weights (grams)

Week	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
Females				
1	126.45±1.27	123.87±0.76	126.56±1.41	125.52±1.39
2	136.97±1.40	131.19±1.19 *	136.01±1.52	134.63±1.40
3	145.08±1.38	139.94±1.36 *	143.92±1.51	143.02±1.63
4	150.51±1.60	144.39±1.27 *	149.37±1.75	148.71±1.72
5	154.88±1.66	148.12±1.22 *	153.41±1.91	153.37±1.90
6	159.91±1.87	152.64±1.09 *	157.00±1.91	159.15±2.09
7	165.00±2.17	154.45±0.98 *	160.72±2.21	163.20±2.14
8	167.85±2.19	156.00±1.17 *	162.91±2.28	165.99±2.38
9	171.37±2.13	158.40±1.27 *	165.79±2.18	169.25±2.40
10	173.81±2.12	160.67±1.23 *	168.08±2.09	172.00±2.51
11	175.51±2.01	161.95±0.85 *	169.39±2.35	173.30±2.79
12	177.97±2.27	163.01±0.52 *	171.28±2.60	175.15±2.87
13	180.04±2.31	163.56±1.02 *	172.35±2.61	177.19±2.83
Males				
1	173.17±1.79	166.74±2.69	170.69±2.59	174.66±3.17
2	193.31±1.99	180.29±3.02 *	190.12±2.65	195.00±3.34
3	213.96±2.65	201.88±3.28 *	212.13±2.99	217.42±3.63
4	228.11±3.21	218.16±3.78	228.42±3.43	231.90±3.60
5	240.14±4.04	232.44±4.05	243.12±3.80	244.78±3.75
6	254.34±4.52	246.20±4.04	257.64±4.24	259.93±4.13
7	268.63±4.99	258.43±4.15	269.30±3.91	273.90±4.56
8	278.63±5.09	266.77±4.31	277.28±3.82	283.12±4.34
9	288.03±5.09	272.90±4.61	285.25±3.47	291.34±4.35
10	296.65±5.06	280.25±4.74 *	293.70±3.66	300.15±4.89
11	304.29±5.17	286.19±5.12 *	301.40±4.01	307.79±5.10
12	312.88±5.06	292.71±5.29 *	308.76±4.03	314.47±4.77
13	319.25±5.29	297.08±5.56 *	313.50±4.23	318.41±4.55

Mean ± Standard Error

*Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 4: Organ Weights (grams)/Females

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
Kidneys	1.25 ± 0.02	1.31 ± 0.01	1.26 ± 0.03	1.30 ± 0.03
Lungs	1.01 ± 0.03	0.96 ± 0.03	0.94 ± 0.02	0.96 ± 0.04
Liver	4.73 ± 0.05	5.13 ± 0.03*	4.97 ± 0.11	4.84 ± 0.10
Heart	0.69 ± 0.02	0.65 ± 0.02	0.64 ± 0.02	0.65 ± 0.02
Brain	1.83 ± 0.02	1.69 ± 0.01*	1.72 ± 0.02*	1.77 ± 0.05
Spleen	0.44 ± 0.01	0.47 ± 0.01	0.44 ± 0.01	0.42 ± 0.01
Adrenals	0.09 ± 0.01	0.07 ± 0.00*	0.07 ± 0.00*	0.08 ± 0.01
Thymus	0.25 ± 0.02	0.19 ± 0.01*	0.22 ± 0.01	0.22 ± 0.01
Gonads	0.17 ± 0.02	0.13 ± 0.01	0.21 ± 0.09	0.14 ± 0.01

Mean ± Standard Error

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 5: Organ Weights (grams)/Males

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
Kidneys	2.20 ± 0.05	2.40 ± 0.05	2.40 ± 0.10	2.29 ± 0.05
Lungs	1.42 ± 0.04	1.41 ± 0.04	1.42 ± 0.07	1.47 ± 0.08
Liver	9.35 ± 0.26	11.03 ± 0.25*	10.07 ± 0.23	9.35 ± 0.22
Heart	1.00 ± 0.02	0.93 ± 0.02	0.96 ± 0.02	1.05 ± 0.03
Brain	1.90 ± 0.02	1.83 ± 0.02*	1.90 ± 0.03	1.92 ± 0.02
Spleen	0.61 ± 0.01	0.71 ± 0.02*	0.63 ± 0.01	0.61 ± 0.01
Adrenals	0.07 ± 0.01	0.07 ± 0.01	0.07 ± 0.00	0.07 ± 0.00
Thymus	0.29 ± 0.02	0.25 ± 0.02	0.26 ± 0.02	0.26 ± 0.01
Gonads	5.08 ± 0.29	4.82 ± 0.17	4.98 ± 0.24	5.37 ± 0.28

Mean ± Standard Error

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 6: Organ-to Body Weight Ratios and Terminal Body Weights/Females

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
Body Weight (grams)	171.55 ±2.13	153.33 ± 1.00*	163.70 ± 2.49*	168.44 ± 2.52
Kidneys (%)	0.73 ± 0.01	0.86 ± 0.01*	0.77 ± 0.01*	0.77 ± 0.01*
Lungs (%)	0.59 ± 0.02	0.62 ± 0.02	0.57 ± 0.01	0.57 ± 0.02
Liver (%)	2.76 ± 0.04	3.35 ± 0.03*	3.04 ± 0.04*	2.87 ± 0.04
Heart (%)	0.40 ± 0.01	0.43 ± 0.02	0.39 ± 0.01	0.38 ± 0.01
Brain (%)	1.07 ± 0.02	1.10 ± 0.01	1.05 ± 0.02	1.06 ± 0.04
Spleen (%)	0.26 ± 0.01	0.30 ± 0.01*	0.27 ± 0.00	0.25 ± 0.00
Adrenals (%)	0.05 ± 0.00	0.05 ± 0.00	0.04 ± 0.00	0.05 ± 0.00
Thymus (%)	0.14 ± 0.01	0.13 ± 0.01	0.13 ± 0.01	0.13 ± 0.01
Gonads (%)	0.10 ± 0.01	0.09 ± 0.00	0.13 ± 0.05	0.08 ± 0.00

Mean ± Standard Error

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 7: Organ-to-Body Weight Ratios and terminal Body Weights/Males

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
Body Weight (grams)	304.19 ± 4.78	279.95 ± 4.71*	297.37 ± 3.89	305.04 ± 4.12
Kidneys (%)	0.72 ± 0.01	0.86 ± 0.01*	0.81 ± 0.04*	0.75 ± 0.01
Lungs (%)	0.47 ± 0.01	0.51 ± 0.01	0.48 ± 0.02	0.48 ± 0.03
Liver (%)	3.07 ± 0.04	3.94 ± 0.03*	3.39 ± 0.04*	3.06 ± 0.05
Heart (%)	0.33 ± 0.01	0.33 ± 0.01	0.32 ± 0.01	0.35 ± 0.01
Brain (%)	0.63 ± 0.01	0.66 ± 0.01	0.64 ± 0.01	0.63 ± 0.01
Spleen (%)	0.20 ± 0.00	0.25 ± 0.00*	0.21 ± 0.00	0.20 ± 0.00
Adrenals (%)	0.02 ± 0.00	0.03 ± 0.00	0.02 ± 0.00	0.02 ± 0.00
Thymus (%)	0.09 ± 0.01	0.09 ± 0.01	0.09 ± 0.01	0.08 ± 0.00
Gonads (%)	1.67 ± 0.09	1.72 ± 0.06	1.67 ± 0.07	1.76 ± 0.08

Mean ± Standard Error

* Significantly different from the control group ($p \leq 0.05$) by Dunnett's test.

Table 8: Hematology Values/Females
45 Days

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
RBC (x10 ⁶ /µL)	8.15 ±0.21	7.80 * ±0.25	7.94 ±0.18	7.99 ±0.16
Hemoglobin (g/dL)	15.66 ±0.25	14.36 * ±0.68	14.66 * ±0.40	14.96 ±0.42
Hematocrit (%)	43.72 ±2.01	42.88 ±1.68	43.78 ±1.83	42.42 ±1.00
WBC (x10 ³ /µL)	4.18 ±0.49	4.78 ±0.73	4.70 ±0.33	4.04 ±0.96
Platelets (x10 ³ /µL)	778.60 ±62.07	796.40 ±82.38	716.6 ±125.3	778.40 ±64.76
Segmented Leukocytes (%)	21.72 ±4.35	12.88 * ±3.36	15.44 ±4.51	19.28 ±4.68
Lymphocytes (%)	74.28 ±5.29	83.68 * ±3.4	80.66 ±4.95	76.50 ±4.57
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
MCV (cumicr)	53.60 ±1.07	54.9 ±.58	55.10 * ±1.26	53.12 ±0.49
MCH (picogm)	19.18 ±0.24	18.38 * ±0.44	18.46 * ±0.39	18.74 ±0.22
MCHC (g/dL)	35.82 ±1.10	33.46 * ±1.06	33.50 * ±1.06	35.26 ±0.28
Reticulocytes (%)	2.02 ±0.25	3.68 * ±0.43	2.32 ±0.11	1.94 ±0.27
MetHb (%)	0.28 ±0.25	1.96 * ±0.41	1.10 * ±0.27	0.90 * ±0.31

Mean ± Standard Deviation

* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 9: Hematology Values/Males
45 Days

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
RBC (x10 ⁶ /µL)	8.66 ±0.12	8.50 ±0.20	8.71 ±0.15	8.87 ±0.30
Hemoglobin (g/dL)	15.44 ±0.29	14.12 * ±0.48	14.90 ±0.43	15.40 ±0.78
Hematocrit (%)	44.90 ±0.97	43.14 ±0.80	43.94 ±1.19	45.20 ±1.71
WBC (x10 ³ /µL)	4.58 ±0.58	4.10 ±0.81	4.20 ±0.87	4.20 ±0.58
Platelets (x10 ³ /µL)	700.60 ±92.44	946.20 * ±73.40	844.20 * ±37.25	789.00 ±34.55
Segmented Leukocytes (%)	19.06 ±4.88	18.94 ±3.48	19.88 ±3.59	20.40 ±2.48
Lymphocytes (%)	78.14 ±4.61	77.84 ±3.31	76.80 ±3.69	76.52 ±2.83
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
MCV (cumicr)	51.88 ±0.53	50.76 * ±0.61	50.46 * ±0.66	50.96 * ±0.28
MCH (picogm)	17.82 ±0.19	16.56 * ±0.23	17.08 * ±0.29	17.34 * ±0.36
MCHC (g/dL)	34.38 ±0.19	32.66 * ±0.58	33.84 ±0.40	34.06 ±0.54
Reticulocytes (%)	2.42 ±0.29	4.16 * ±0.15	2.84 ±0.26	2.26 ±0.34
MetHb (%)	0.42 ±0.31	2.44 * 0.46	1.36 * ±0.33	0.88 ±0.48

Mean ± Standard Deviation

* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 10: Hematology Values/Females
90 Days

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
RBC ($\times 10^6/\mu\text{L}$)	8.24 ± 0.21	7.70 * ± 0.34	8.12 ± 0.19	8.23 ± 0.27
Hemoglobin (g/dL)	15.66 ± 0.35	14.53 * ± 0.44	15.18 * ± 0.32	15.66 ± 0.58
Hematocrit (%)	44.61 ± 1.58	43.22 ± 1.49	43.85 ± 1.41	44.55 ± 1.82
WBC ($\times 10^3/\mu\text{L}$)	4.14 ± 0.70	3.71 ± 0.56	3.69 ± 0.57	3.41 * ± 0.57
Platelets ($\times 10^3/\mu\text{L}$)	742.50 ± 32.03	853.40 * ± 53.81	811.40 * ± 71.07	758.10 ± 60.50
Segmented Leukocytes (%)	19.82 ± 3.37	18.27 ± 3.33	22.33 ± 2.11	20.27 ± 4.84
Lymphocytes (%)	75.75 ± 3.70	77.42 ± 4.34	73.21 ± 2.44	75.49 ± 5.24
Heinz Bodies (%)	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00	0.0 ± 0.00
MCV (cumicr)	54.14 ± 0.82	55.56 * ± 1.21	54.01 ± 0.78	54.14 ± 0.94
MCH (picogm)	19.01 ± 0.43	18.68 ± 0.30	18.70 ± 0.24	19.05 ± 0.37
MCHC (g/dL)	35.13 ± 1.04	33.67 * ± 0.94	34.62 ± 0.81	35.20 ± 0.82
Reticulocytes (%)	1.71 ± 0.28	2.63 * ± 0.37	2.06 * ± 0.28	1.77 ± 0.22
MetHb (%)	0.59 ± 0.33	2.23 * ± 0.34	1.09 * ± 0.33	0.68 ± 0.33

Mean \pm Standard Deviation

* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 11: Hematology Values/Males
90 Days

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
RBC (x10 ⁶ /µL)	9.34 ±0.19	8.94 * ±0.18	9.27 ±0.18	9.31 ±0.23
Hemoglobin (g/dL)	15.83 ±0.23	14.22 * ±0.25	15.31 * ±0.23	15.61 ±0.41
Hematocrit (%)	48.37 ±0.79	44.98 * ±0.95	47.15 * ±1.23	48.05 ±1.14
WBC (x10 ³ /µL)	4.35 ±0.64	4.43 ±0.58	4.30 ±0.63	4.21 ±0.68
Platelets (x10 ³ /µL)	733.70 ±87.65	856.70 * ±45.82	745.10 ±83.61	728.30 ±43.06
Segmented Leukocytes (%)	22.38 ±3.75	24.96 ±1.84	25.84 ±4.22	22.55 ±3.55
Lymphocytes (%)	73.31 ±4.35	71.16 ±2.88	69.29 ±4.67	72.87 ±3.73
Heinz Bodies (%)	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00	0.0 ±0.00
MCV (cumicr)	51.81 ±0.81	50.30 * ±0.77	50.85 * ±0.70	51.61 ±0.69
MCH (picogm)	16.94 ±0.24	15.92 * ±0.16	16.51 * ±0.16	16.76 ±0.41
MCHC (g/dL)	32.73 ±0.52	31.64 * ±0.61	32.45 ±0.46	32.51 ±0.85
Reticulocytes (%)	1.96 ±0.19	3.35 * ±0.18	2.05 ±0.13	1.88 ±0.20
MetHb (%)	0.50 ±0.40	2.67 * ±0.54	1.37 * 0.27	0.58 ±0.32

Mean ± Standard Deviation

* Significantly different from the control group ($P \leq 0.05$) by the Dunnett's test.

Table 12: Clinical Chemistry Values/Females
45 Days

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
Glucose (mg/dl)	154.80 ± 21.04	130.20 ± 20.35	161.40 ± 17.87	166.00 ± 5.00
BUN (mg/dl)	18.40 ± 3.21	17.20 ± 1.92	17.00 ± 1.00	17.60 ± 1.67
Creatinine (mg/dl)	0.52 ± 0.04	0.60 ± 0.00*	0.64 ± 0.05*	0.54 ± 0.05
Alk phos (IU/L)	123.20 ± 10.83	116.00 ± 16.84	122.40 ± 24.57	122.60 ± 26.31
AST (IU/L)	106.20 ± 26.44	147.20 ± 33.94	182.20 ± 92.88	95.20 ± 11.12
ALT (IU/L)	37.40 ± 4.28	38.20 ± 6.38	60.20 ± 35.15	35.60 ± 5.68
Potassium (mEq/L)	4.58 ± 0.37	4.54 ± 0.45	4.30 ± 0.16	4.52 ± 0.49
Albumin (g/dl)	4.38 ± 0.08	4.58 ± 0.33	4.68 ± 0.13	4.22 ± 0.16
Calcium (mg/dl)	10.66 ± 0.21	10.70 ± 0.21	10.96 ± 0.13	10.60 ± 0.20
Phosphorus (mg/dl)	8.90 ± 1.27	9.44 ± 1.69	10.02 ± 1.42	8.38 ± 0.52
Triglycerides (mg/dl)	39.60 ± 8.82	29.40 ± 3.58	47.60 ± 14.54	38.80 ± 10.85
Sodium (mEq/L)	138.40 ± 1.67	139.60 ± 0.55	139.60 ± 1.82	138.60 ± 0.55
Total Bilirubin (mg/dl)	0.18 ± 0.04	0.26 ± 0.05*	0.20 ± 0.00	0.14 ± 0.05
Total Protein (g/dl)	6.20 ± 0.32	6.28 ± 0.04	6.52 ± 0.08	6.04 ± 0.15

Mean ± Standard Deviation

* Significantly different from controls; p ≤ 0.05 by Dunnett's test.

Table 13: Clinical Chemistry Values/Males
45 Days

	Dose Groups (mg tetryl/kg diet)			
	0	3000	1000	200
Glucose (mg/dl)	194.60 ± 21.85	175.20 ± 9.65	185.20 ± 19.61	183.60 ± 15.88
BUN (mg/dl)	19.60 ± 1.52	18.00 ± 1.22	20.40 ± 1.52	18.40 ± 3.13
Creatinine (mg/dl)	0.60 ± 0.07	0.60 ± 0.00	0.62 ± 0.04	0.56 ± 0.05
Alk phos (IU/L)	135.80 ± 8.78	119.60 ± 12.56	123.80 ± 10.03	134.00 ± 14.61
AST (IU/L)	126.80 ± 16.18	111.60 ± 19.83	134.40 ± 39.30	113.60 ± 12.22
ALT (IU/L)	53.80 ± 12.68	38.60 ± 8.56	51.60 ± 23.20	45.80 ± 6.80
Potassium (mEq/L)	4.74 ± 0.51	5.62 ± 0.54*	4.82 ± 0.44	4.70 ± 0.59
Albumin (g/dl)	4.38 ± 0.08	5.04 ± 0.09*	4.78 ± 0.16*	4.64 ± 0.26
Calcium (mg/dl)	10.64 ± 0.15	11.14 ± 0.15*	11.02 ± 0.16*	10.80 ± 0.07
Phosphorus (mg/dl)	9.82 ± 0.52	10.82 ± 1.01	9.84 ± 0.43	9.64 ± 0.60
Triglycerides (mg/dl)	99.80 ± 23.55	64.20 ± 24.80	97.00 ± 28.22	88.60 ± 44.81
Sodium (mEq/dl)	137.60 ± 1.52	138.40 ± 0.55	139.00 ± 1.22	139.00 ± 1.00
Total Bilirubin (mg/dl)	0.14 ± 0.09	0.18 ± 0.04	0.12 ± 0.04	0.14 ± 0.09
Total Protein (g/dl)	6.30 ± 0.14	7.12 ± 0.18*	6.88 ± 0.13*	6.60 ± 0.21*

Mean ± Standard Deviation

* Significantly different from controls; p ≤ 0.05 by Dunnett's test.

Table 14: Clinical Chemistry Values/Females
90 Days

	Dose groups (mg tetryl/kg diet)			
	0	3000	1000	200
Glucose (mg/dl)	125.10 ± 17.64	130.00 ± 17.31	145.30 ± 18.66*	138.80 ± 15.42
BUN (mg/dl)	18.30 ± 2.21	20.20 ± 2.97	20.20 ± 2.39	19.00 ± 1.89
Creatinine (mg/dl)	0.54 ± 0.05	0.57 ± 0.05	0.56 ± 0.05	0.55 ± 0.05
Alk phos (IU/L)	76.50 ± 11.40	63.30 ± 9.35*	67.90 ± 8.02	74.00 ± 15.32
AST (IU/L)	132.00 ± 27.94	159.30 ± 33.04	160.70 ± 37.69	180.20 ± 65.81*
ALT (IU/L)	55.20 ± 19.23	59.00 ± 16.42	79.80 ± 30.14	85.40 ± 46.21
Potassium (mEq/L)	4.03 ± 0.25	4.56 ± 0.86	4.48 ± 0.45	4.49 ± 0.50
Albumin (g/dl)	4.42 ± 0.15	4.96 ± 0.21*	4.72 ± 0.12*	4.67 ± 0.23*
Calcium (mg/dl)	10.04 ± 0.24	10.34 ± 0.43	10.18 ± 0.21	10.23 ± 0.23
Phosphorus (mg/dl)	8.31 ± 0.97	9.12 ± 0.99	8.57 ± 0.98	8.63 ± 1.10
Triglycerides (mg/dl)	40.60 ± 13.93	25.40 ± 3.86*	36.20 ± 13.31	44.60 ± 15.14
Cholesterol (mg/dl)	102.70 ± 6.80	131.50 ± 10.22*	123.00 ± 8.91*	112.90 ± 8.85*
Sodium (mEq/L)	142.70 ± 0.82	143.50 ± 1.08	142.80 ± 1.14	142.90 ± 0.74
Total Bilirubin (mg/dl)	0.11 ± 0.03	0.22 ± 0.04*	0.16 ± 0.07	0.19 ± 0.10*
Total Protein (g/dl)	6.18 ± 0.19	6.71 ± 0.33*	6.52 ± 0.20*	6.37 ± 0.28

Mean ± Standard Deviation

* Significantly different from controls; p ≤ 0.05 by Dunnett's test.

Table 15: Clinical Chemistry Values/Males
90 Days

	Dose groups (mg tetryl/kg diet)			
	0	3000	1000	200
Glucose (mg/dl)	185.60 ± 18.06	180.10 ± 17.99	187.50 ± 15.66	187.50 ± 19.46
BUN (mg/dl)	20.20 ± 0.92	21.00 ± 1.15	22.20 ± 1.03*	20.60 ± 2.22
Creatinine (mg/dl)	0.62 ± 0.04	0.60 ± 0.05	0.61 ± 0.03	0.62 ± 0.04
Alk phos (IU/L)	104.90 ± 6.87	80.90 ± 6.38*	88.30 ± 8.71*	93.70 ± 6.60*
AST (IU/L)	157.00 ± 43.60	175.50 ± 30.75	164.60 ± 21.88	150.30 ± 29.70
ALT (IU/L)	85.10 ± 28.73	66.50 ± 11.00	80.40 ± 16.30	83.80 ± 17.78
Potassium (mEq/L)	4.65 ± 0.31	5.00 ± 0.24	4.62 ± 0.38	4.80 ± 0.38
Albumin (g/dl)	4.72 ± 0.16	5.12 ± 0.21*	5.00 ± 0.11*	4.82 ± 0.12
Calcium (mg/dl)	10.47 ± 0.12	10.70 ± 0.21*	10.67 ± 0.18*	10.60 ± 0.18
Phosphorus (mg/dl)	9.05 ± 0.55	8.97 ± 0.89	8.59 ± 0.97	8.95 ± 0.66
Triglycerides (mg/dl)	104.40 ± 27.63	89.30 ± 32.15	119.40 ± 28.89	103.40 ± 30.56
Cholesterol (mg/dl)	58.60 ± 7.06	105.40 ± 7.57*	79.10 ± 4.65*	66.40 ± 4.77*
Sodium (mEq/L)	143.00 ± 0.94	142.30 ± 0.67	143.00 ± 0.82	143.50 ± 1.08
Total Bilirubin (mg/dl)	0.05 ± 0.05	0.10 ± 0.00*	0.09 ± 0.03*	0.10 ± 0.00*
Total Protein (g/dl)	6.81 ± 0.21	7.39 ± 0.30*	7.22 ± 0.23*	6.88 ± 0.13

Mean ± Standard Deviation

* Significantly different from controls; $p \leq 0.05$ by Dunnett's test.

APPENDIX A

**FOOD AND WATER
CONSUMPTION**

Weekly Food Consumption
Group Means

Group	Sex	Diet Concentration (mg tetryl/kg)	Food (g/wk)		
			Week 11	Week 12	Week 13
1	F	0	84.67 ± 2.38	85.79 ± 2.37	45.64 ± 0.93
2	F	3000	71.38 ± 1.39	70.63 ± 1.42	39.20 ± 1.03
3	F	1000	71.54 ± 3.64	74.90 ± 1.45	41.65 ± 0.72
4	F	200	78.83 ± 1.80	81.01 ± 1.84	44.29 ± 1.07
5	M	0	125.02 ± 3.00	128.00 ± 2.54	85.68 ± 2.84
6	M	3000	107.11 ± 2.95	110.14 ± 1.72	75.92 ± 1.69
7	M	1000	113.66 ± 2.27	116.94 ± 1.20	80.51 ± 1.57
8	M	200	123.16 ± 1.99	128.90 ± 2.22	85.17 ± 1.53

* Mean ± Standard Error

Week 13 is for 5 days only

**Weekly Food Consumption
Group Means**

Group	Sex	Concentration (mg tetryl/kg)	Diet	Food (g/wk)				
			Week 1	Week 2	Week 3	Week 4	Week 5	
1	F	0	106.15 ± 1.47	79.64 ± 1.01	84.82 ± 1.10	85.64 ± 1.20	84.92 ± 2.43	
2	F	3000	84.92 ± 2.07	70.59 ± 0.70	72.79 ± 1.37	75.25 ± 1.36	72.63 ± 1.90	
3	F	1000	101.75 ± 1.97	75.42 ± 0.94	77.83 ± 1.25	79.43 ± 1.72	74.99 ± 2.06	
4	F	200	103.16 ± 1.43	77.78 ± 1.04	80.93 ± 1.99	84.11 ± 1.32	82.63 ± 1.43	
5	M	0	139.91 ± 2.15	116.07 ± 2.19	118.43 ± 2.45	119.67 ± 2.89	121.65 ± 3.19	
6	M	3000	111.38 ± 2.48	99.29 ± 2.30	101.16 ± 2.02	103.54 ± 2.04	101.16 ± 2.28	
7	M	1000	124.33 ± 1.63	107.04 ± 1.94	110.90 ± 1.54	111.89 ± 1.82	110.29 ± 2.01	
8	M	200	135.09 ± 2.00	112.01 ± 2.07	114.96 ± 1.09	119.13 ± 1.75	116.91 ± 1.93	

Week 1 is for 6 days only

Group	Sex	Diet	Food (g/wk)				
		Concentration (mg tetryl/kg)	Week 6	Week 7	Week 8	Week 9	Week 10
1	F	0	80.77 ± 1.35	85.99 ± 1.30	87.26 ± 1.27	85.46 ± 0.94	81.61 ± 1.39
2	F	3000	70.07 ± 0.89	73.05 ± 1.14	71.89 ± 0.90	72.75 ± 0.66	71.00 ± 1.28
3	F	1000	74.63 ± 2.39	78.58 ± 1.30	77.86 ± 1.52	76.06 ± 1.58	72.89 ± 1.54
4	F	200	81.87 ± 1.31	82.18 ± 1.45	80.87 ± 1.93	82.31 ± 2.18	75.60 ± 1.77
5	M	0	119.76 ± 3.51	128.07 ± 3.26	129.04 ± 2.76	124.11 ± 2.75	123.85 ± 2.88
6	M	3000	102.77 ± 2.05	106.35 ± 1.88	106.65 ± 1.90	106.48 ± 1.59	103.99 ± 2.66
7	M	1000	111.04 ± 1.46	114.62 ± 1.35	115.13 ± 1.29	112.96 ± 1.33	112.70 ± 2.05
8	M	200	120.95 ± 2.19	125.65 ± 1.87	125.48 ± 2.54	121.70 ± 2.90	122.03 ± 2.35

* Mean ± Standard Error

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1*	Week 2	Week 3	Week 4	Week 5	Week 1*	Week 2	Week 3	Week 4	Week 5
1	1	83.8	68.7	74.3	71.7	73.4	130.1	130.9	139.9	143.5	148.7
	2	85.0	69.9	70.8	74.5	82.9	155.5	137.1	124.9	163.6	161.2
	3	81.9	70.4	75.0	80.5	74.0	129.7	103.1	101.2	113.7	109.0
	4	88.0	74.6	69.9	75.5	69.7	154.3	127.9	119.9	148.1	159.2
	5	92.5	69.6	79.2	77.2	72.3	155.7	134.4	123.0	127.2	140.8
	6	96.2	74.6	77.9	80.7	67.2	153.5	140.3	113.4	125.6	126.7
	7	86.2	69.3	69.3	77.7	75.6	157.9	138.2	140.1	156.6	153.9
	8	82.8	69.9	75.5	76.2	79.7	145.3	122.6	127.6	139.4	143.7
	9	72.6	68.3	65.0	71.8	69.4	149.7	138.3	141.4	132.1	150.4
	10	80.2	70.6	71.0	66.7	62.1	136.0	115.6	117.1	123.1	127.6
2	11	103.9	80.8	82.8	89.9	80.5	161.1	135.4	125.5	130.3	125.6
	12	93.1	76.4	74.5	82.8	73.4	180.3	132.1	130.0	141.0	134.7
	13	105.1	73.4	72.4	76.2	78.9	151.8	116.4	117.6	127.1	119.8
	14	95.5	71.9	73.2	79.3	75.3	167.5	127.4	122.0	130.6	122.0
	15	106.6	74.3	76.5	77.2	65.6	101.8	123.9	121.0	112.0	118.0
	16	99.2	73.9	80.9	76.9	63.2	160.4	115.4	124.3	133.2	119.2
	17	104.9	73.9	78.7	80.9	78.4	150.7	129.6	140.0	144.3	155.6
	18	96.7	75.9	77.3	75.3	76.3	168.3	133.0	124.1	139.1	135.2
	19	113.8	80.2	84.2	85.0	84.6	186.4	148.2	141.9	137.9	139.6
	20	98.7	73.5	77.8	70.8	73.7	148.2	105.0	96.2	101.6	105.3

*Week 1 is only 6 days

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
1	1	70.7	75.2	69.6	73.0	74.1	146.6	154.8	143.3	168.4	164.5
	2	75.1	69.5	76.2	74.3	70.6	174.7	159.8	175.3	177.1	171.8
	3	69.6	76.1	74.9	72.9	76.5	116.5	124.4	113.7	112.4	115.1
	4	67.9	73.2	73.8	76.9	77.8	157.9	129.5	145.0	156.0	150.3
	5	74.7	73.8	74.0	73.4	70.0	134.2	135.0	135.5	147.6	142.6
	6	70.8	69.7	69.5	71.3	66.8	121.3	116.5	123.5	128.2	124.3
	7	68.8	80.1	69.3	69.7	66.6	158.0	157.7	149.4	156.6	152.4
	8	68.0	74.3	73.6	73.8	72.1	135.4	142.8	136.1	144.0	145.4
	9	68.1	69.6	68.8	71.7	67.7	151.3	152.9	147.2	155.7	171.4
	10	67.0	69.0	69.2	70.5	67.8	126.5	133.6	143.0	138.0	137.2
2	11	78.7	79.5	76.4	81.2	75.7	119.3	121.2	117.4	123.3	119.4
	12	74.4	80.9	78.2	79.7	77.6	138.4	143.5	142.7	150.6	132.8
	13	76.2	74.7	86.4	78.7	72.6	119.5	130.3	126.5	125.8	115.4
	14	76.3	81.4	78.8	79.4	71.7	133.0	145.3	135.5	146.4	145.2
	15	72.1	76.3	76.2	72.7	71.5	119.7	128.9	128.3	133.8	124.8
	16	64.8	82.2	77.6	75.9	72.6	90.9	127.2	111.9	119.3	111.6
	17	75.5	79.8	79.9	77.9	76.5	139.4	150.2	132.1	142.4	135.9
	18	74.9	75.6	73.7	71.8	66.2	142.4	139.5	127.5	139.6	128.4
	19	90.5	84.5	82.7	78.5	80.0	137.0	145.0	149.5	145.3	143.7
	20	62.9	70.9	68.7	64.8	64.5	96.3	105.8	105.3	100.3	101.4

Individual Food and Water Consumption

Females

Group	Animal Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	Week 13*
1	1	77.7	77.1	32.8	162.9	153.3	78.4
	2	68.5	67.8	38.4	182.7	188.8	108.4
	3	70.2	70.3	38.4	112.3	108.8	65.4
	4	71.3	74.6	39.8	149.1	130.3	71.0
	5	75.3	75.5	44.2	144.6	141.2	84.5
	6	74.7	67.5	36.1	115.4	119.0	73.3
	7	75.0	70.6	43.0	147.3	162.0	86.0
	8	70.0	72.7	39.6	138.4	154.6	78.9
	9	62.9	62.1	41.0	160.4	160.6	80.0
	10	68.2	68.1	38.7	145.4	141.3	80.7
2	11	82.2	77.9	41.1	123.9	125.4	66.2
	12	79.0	77.3	43.0	130.9	139.5	71.6
	13	73.0	74.7	43.6	118.8	123.9	80.4
	14	72.8	78.6	43.1	145.1	156.5	87.1
	15	78.1	74.4	44.3	125.7	136.4	73.1
	16	78.0	74.3	38.5	111.3	117.1	66.1
	17	44.2	78.5	41.8	149.4	137.8	78.1
	18	70.8	69.0	39.4	123.8	132.4	78.7
	19	77.9	79.1	43.6	140.1	141.9	79.7
	20	59.4	65.2	38.1	96.5	102.4	63.6

*Week 13 is only 5 days

Individual Food and Water Consumption

Females

Food (g/wk)

Water (g/wk)

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1*	Week 2	Week 3	Week 4	Week 5	Week 1*	Week 2	Week 3	Week 4	Week 5
3	21	107.9	77.8	84.2	81.7	77.6	177.1	120.6	111.2	121.8	120.4
	22	103.1	77.9	84.2	86.6	85.7	155.8	119.4	114.9	117.3	115.8
	23	107.5	80.7	82.8	83.6	85.2	168.1	120.3	127.6	134.7	131.7
	24	106.9	83.6	83.6	85.5	86.9	179.3	124.7	123.9	129.4	134.1
	25	98.8	73.7	77.7	79.4	84.6	164.0	123.5	111.8	121.5	120.6
	26	107.2	80.5	86.5	89.4	84.8	163.5	119.2	117.8	129.2	130.2
	27	103.0	76.3	81.8	90.3	86.5	153.8	115.6	121.6	125.7	128.1
	28	96.5	73.7	76.6	80.9	77.9	160.6	124.9	120.3	124.2	128.8
	29	104.5	79.0	86.3	86.0	83.3	172.8	135.4	135.1	121.9	123.2
	30	96.2	74.6	65.6	77.7	73.8	164.4	127.3	124.1	118.4	116.4
4	31	110.3	79.5	87.0	89.8	96.1	192.7	154.3	145.0	146.4	153.0
	32	115.3	82.8	85.7	89.8	88.8	181.5	131.4	131.4	124.0	122.8
	33	98.1	81.2	82.9	84.2	79.0	169.5	129.3	121.7	116.9	116.3
	34	105.6	76.2	84.8	80.3	87.2	173.0	136.1	123.4	114.1	113.4
	35	107.2	78.7	85.0	89.9	81.7	186.1	144.0	131.7	128.5	115.3
	36	103.6	74.0	81.8	79.6	84.1	164.6	126.7	115.1	109.2	116.9
	37	105.5	79.6	83.7	87.3	78.1	157.0	116.6	121.7	119.3	122.4
	38	104.7	85.6	90.9	86.8	89.2	164.7	129.9	121.3	121.0	129.8
	39	102.6	79.4	88.1	85.2	94.0	169.1	124.3	129.8	129.8	126.9
	40	108.6	79.4	78.3	83.5	71.0	173.5	125.7	108.4	107.0	108.6

*Week 1 is only 6 days

Individual Food and Water Consumption

Females

Animal Group	Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
3	21	79.1	76.2	79.5	77.8	73.3	117.9	111.2	109.5	119.1	114.8
	22	85.1	81.6	79.9	80.9	76.3	117.1	116.5	111.9	116.1	103.3
	23	85.2	84.5	84.3	83.4	77.7	132.6	135.9	122.7	116.7	120.4
	24	82.5	84.1	84.0	88.0	85.0	126.9	131.6	133.0	132.3	136.1
	25	76.3	74.8	70.5	72.3	65.9	123.9	127.6	124.8	127.6	120.7
	26	89.0	88.4	88.8	90.5	78.5	133.1	137.6	138.9	141.3	128.5
	27	83.5	88.9	86.5	92.5	77.8	133.5	135.4	132.8	137.8	121.2
	28	79.6	81.4	81.1	79.2	73.2	124.9	131.7	128.7	129.3	123.4
	29	82.4	82.2	83.4	85.2	79.9	131.4	126.8	125.4	131.7	129.1
	30	76.0	79.7	70.7	73.3	68.4	115.4	118.8	119.0	117.5	123.5
4	31	89.4	92.0	91.7	85.8	85.8	153.4	144.3	147.7	147.8	154.1
	32	83.2	93.9	90.9	93.0	89.8	118.7	132.7	125.7	130.1	132.9
	33	74.5	84.6	83.6	84.1	82.8	116.6	117.7	112.4	113.4	112.8
	34	81.9	84.1	80.6	83.5	77.3	118.9	121.9	107.8	114.6	108.0
	35	81.9	88.1	84.8	85.3	80.4	122.8	124.9	118.1	122.7	119.1
	36	75.0	83.1	84.0	84.3	75.8	111.8	114.5	121.5	116.1	110.0
	37	80.2	85.8	86.9	84.1	85.5	115.7	122.8	114.4	119.3	112.8
	38	82.6	81.3	87.1	86.6	79.7	118.1	115.1	115.1	122.7	119.7
	39	80.0	84.2	92.1	82.0	81.3	126.6	129.3	109.3	131.1	126.2
	40	79.0	82.8	90.9	85.9	77.7	103.9	103.4	116.3	111.0	109.7

Individual Food and Water Consumption

Females

Animal Group	Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	Week 13*
3	21	80.3	79.6	46.2	112.6	123.7	59.9
	22	80.9	78.6	44.3	101.2	109.6	59.4
	23	75.5	76.3	40.9	113.4	109.8	60.0
	24	80.8	92.8	47.2	127.5	142.6	74.9
	25	74.9	79.4	37.0	120.4	126.4	68.3
	26	85.0	82.0	47.6	134.0	134.2	79.9
	27	73.9	85.7	44.1	124.1	117.9	70.4
	28	81.4	84.0	45.0	126.3	134.4	72.1
	29	87.4	80.7	47.8	119.4	127.7	78.3
	30	68.2	71.0	42.8	125.2	135.8	77.8
4	31	91.3	88.9	49.4	144.4	141.3	83.8
	32	80.5	100.6	48.4	125.6	131.1	65.4
	33	79.1	80.4	43.8	110.1	113.9	62.3
	34	74.4	78.5	39.3	107.1	105.3	48.9
	35	92.5	90.3	44.1	119.6	127.3	43.3
	36	74.6	79.8	46.4	104.8	112.3	61.9
	37	92.6	93.8	48.2	118.2	126.6	58.9
	38	86.7	86.0	45.2	118.8	125.5	66.9
	39	81.8	79.2	44.8	131.8	122.2	77.1
	40	93.2	80.4	46.8	113.5	109.1	58.1

*Week 13 is only 5 days

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1*	Week 2	Week 3	Week 4	Week 5	Week 1*	Week 2	Week 3	Week 4	Week 5
5	41	107.1	99.5	101.9	108.7	97.9	178.7	170.6	160.0	156.1	153.2
	42	116.5	111.7	108.0	105.3	102.5	184.6	179.2	180.0	179.7	177.0
	43	121.9	97.7	100.8	105.2	106.0	165.0	145.5	149.1	159.1	150.6
	44	115.7	102.6	106.3	110.7	104.9	179.7	174.2	166.0	180.6	170.5
	45	96.5	92.0	94.1	91.0	90.0	150.4	138.4	124.2	125.0	126.2
	46	120.3	104.3	103.8	107.0	110.5	178.5	166.6	165.5	159.9	164.9
	47	113.0	98.4	105.3	106.0	109.1	177.8	159.0	149.9	161.1	161.2
	48	111.3	105.2	106.1	108.1	104.2	164.2	169.5	162.8	150.4	146.2
	49	103.3	85.9	97.6	97.3	91.4	145.2	134.6	144.1	137.9	141.7
	50	108.2	95.6	87.7	96.1	95.1	159.2	172.8	174.0	180.9	178.0
6	51	126.3	115.3	113.3	110.7	109.8	214.2	195.9	199.7	189.6	181.4
	52	130.8	110.1	108.3	116.2	115.2	188.3	168.6	151.6	160.4	162.0
	53	126.1	109.7	108.9	113.7	116.7	197.0	177.6	172.0	176.2	167.0
	54	128.7	103.3	111.8	113.0	111.0	188.6	164.7	159.9	154.7	157.5
	55	124.4	107.2	114.8	107.6	106.4	179.3	152.3	165.0	153.4	156.7
	56	118.9	99.1	101.3	97.9	99.5	177.3	152.7	142.3	127.8	126.6
	57	118.7	108.7	110.1	112.5	109.3	190.9	168.6	163.8	154.6	154.2
	58	129.1	116.0	119.6	117.7	120.1	189.1	169.7	171.6	171.1	169.2
	59	115.1	102.4	108.0	112.7	112.6	167.2	153.1	155.7	151.2	154.5
	60	125.2	98.6	112.9	116.9	102.3	189.3	168.3	167.1	154.7	143.8

Week 1 is only 6 days

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
5	41	107.6	102.5	104.1	105.6	106.4	160.8	148.6	168.0	170.8	170.0
	42	101.5	105.5	100.1	107.9	105.6	186.4	188.3	190.2	185.6	177.5
	43	106.8	106.1	110.9	106.1	101.2	149.1	142.5	151.6	159.5	147.8
	44	101.8	109.4	113.5	105.4	105.3	175.3	172.3	173.7	154.4	153.2
	45	96.7	103.7	104.7	106.5	100.0	128.3	126.5	124.9	129.3	132.1
	46	115.3	120.5	113.6	116.0	121.5	171.1	177.8	171.4	180.7	183.1
	47	101.8	103.9	107.5	105.8	101.0	153.4	161.3	163.8	155.8	146.9
	48	106.4	110.3	113.6	112.0	108.1	154.0	144.8	164.7	155.1	149.7
	49	96.6	99.9	99.2	102.1	103.3	137.8	131.6	125.9	139.7	130.9
	50	93.2	101.7	99.3	97.4	87.5	174.6	165.3	167.5	156.4	116.5
6	51	108.0	120.7	110.2	109.8	112.3	180.0	175.1	169.0	177.1	164.3
	52	114.2	117.7	115.9	116.8	118.7	158.9	154.6	153.1	149.9	152.3
	53	114.4	114.1	112.6	114.2	114.5	158.4	162.4	156.0	156.4	160.2
	54	108.5	116.5	116.9	115.2	112.6	151.0	153.1	154.3	154.4	147.9
	55	111.9	111.5	111.3	111.5	107.2	156.2	151.6	154.2	147.9	151.9
	56	106.5	109.4	112.3	109.2	103.8	129.1	135.3	142.6	145.5	144.4
	57	113.4	115.5	111.8	110.5	115.1	150.8	150.4	148.2	149.3	153.6
	58	119.8	118.7	122.0	121.0	125.6	165.2	165.0	154.5	159.6	162.2
	59	109.7	115.1	117.9	114.6	111.9	150.5	162.5	156.4	153.6	156.2
	60	104.0	107.0	120.4	106.8	105.3	135.6	132.9	143.2	133.3	138.5

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	*Week 13
5	41	90.3	111.7	74.0	173.4	186.9	**
	42	106.2	107.8	72.3	183.5	183.9	48.3
	43	109.0	116.2	74.3	155.7	152.3	58.1
	44	104.5	111.7	71.7	160.2	154.9	41.2
	45	104.3	104.4	77.8	123.1	135.3	49.3
	46	124.2	116.1	86.9	181.8	183.6	37.5
	47	110.9	116.9	75.7	150.4	165.4	52.2
	48	117.7	108.5	82.6	153.2	147.3	43.7
	49	104.5	107.8	75.1	123.8	131.6	30.6
	50	99.5	100.3	68.8	144.3	152.1	77.4
6	51	106.4	115.5	81.2	177.1	185.5	108.8
	52	117.6	120.2	89.3	147.7	147.1	90.7
	53	116.3	116.2	80.8	160.3	158.1	84.4
	54	108.3	119.3	78.1	143.2	155.2	84.2
	55	105.4	118.8	75.2	146.3	152.3	87.6
	56	117.3	117.3	80.0	145.2	148.9	67.1
	57	105.6	111.4	82.3	150.2	151.2	54.5
	58	127.8	123.7	85.6	159.0	167.5	71.8
	59	114.6	115.5	81.1	159.8	163.3	72.4
	60	117.3	111.5	71.5	141.5	138.3	76.3

*Week 13 is only 5 days, ** Data unavailable

Individual Food and Water Consumption

Males

Food (g/wk)

Water (g/wk)

Group	Animal Number	Food (g/wk)					Water (g/wk)				
		Week 1*	Week 2	Week 3	Week 4	Week 5	Week 1*	Week 2	Week 3	Week 4	Week 5
7	61	145.0	128.8	120.4	130.2	126.7	222.2	198.0	193.0	187.1	190.8
	62	138.7	115.2	115.8	120.1	123.1	196.3	167.0	150.3	167.2	170.3
	63	128.1	109.4	116.1	117.4	114.0	180.8	152.8	149.3	144.7	161.9
	64	135.5	110.2	111.1	121.5	114.4	197.6	168.5	158.3	155.3	151.1
	65	135.2	109.4	113.2	120.5	121.8	205.5	159.4	152.7	146.6	144.7
	66	135.0	113.8	113.7	112.9	112.6	182.7	167.6	164.1	152.1	151.1
	67	137.7	109.3	118.1	120.3	122.7	177.3	147.6	141.5	149.0	161.2
	68	141.9	111.3	118.6	122.6	114.0	201.7	172.5	159.9	155.3	151.9
	69	124.3	106.3	113.1	115.4	111.4	222.9	187.8	187.1	169.4	179.0
	70	129.5	106.4	109.5	110.4	108.4	196.7	153.6	142.1	149.5	136.2
8	71	136.1	102.2	110.8	127.4	130.9	180.1	137.6	143.5	143.8	147.4
	72	139.6	118.6	119.4	126.5	132.2	204.6	157.8	169.7	166.3	173.5
	73	151.0	112.2	119.7	124.0	121.3	200.7	163.0	149.3	145.9	159.9
	74	150.7	128.7	124.8	121.9	128.6	221.0	178.6	167.9	168.5	162.6
	75	140.5	118.6	121.7	126.5	131.3	197.6	174.4	169.4	168.3	174.2
	76	131.8	119.5	123.2	117.2	121.6	176.5	145.2	154.8	139.9	159.0
	77	131.2	110.3	99.6	99.0	104.9	172.0	149.1	133.7	118.6	124.0
	78	138.2	116.3	118.6	110.9	105.3	181.7	150.5	146.5	127.8	136.9
	79	137.0	115.6	122.0	127.0	123.7	198.7	177.6	180.6	172.1	174.2
	80	143.0	118.7	124.5	116.3	116.7	190.2	159.2	155.3	148.8	144.1

Week 1 is only 6 days

Individual Food and Water Consumption

Males

Animal Group	Number	Food (g/wk)					Water (g/wk)				
		Week 6	Week 7	Week 8	Week 9	Week 10	Week 6	Week 7	Week 8	Week 9	Week 10
7	61	131.0	129.4	142.5	137.6	128.1	180.7	197.2	191.9	186.8	171.3
	62	125.0	127.0	122.6	127.8	124.1	168.6	164.5	170.5	169.9	163.4
	63	115.6	122.9	117.7	121.4	122.8	154.9	150.0	158.9	154.5	154.9
	64	117.0	121.8	122.8	119.8	121.1	162.2	161.1	170.0	164.2	157.0
	65	122.8	127.4	122.5	107.3	126.6	147.5	148.8	147.4	117.6	146.3
	66	123.2	132.3	128.8	119.7	124.6	154.3	164.5	162.0	156.8	155.3
	67	128.7	134.0	133.7	129.8	129.5	168.8	165.8	161.1	164.2	165.0
	68	123.9	127.9	128.5	127.5	126.1	151.5	158.5	154.8	148.0	145.4
	69	111.4	116.8	117.6	112.0	108.4	178.0	170.1	171.5	175.1	157.7
	70	110.9	117.0	118.1	114.1	109.0	145.6	159.3	147.8	143.6	145.3
8	71	137.7	135.8	126.9	122.8	129.2	160.6	153.4	149.2	137.0	143.5
	72	128.8	132.1	136.6	128.2	130.1	169.0	175.2	164.4	162.9	165.9
	73	123.6	132.8	130.6	125.9	128.3	152.3	160.3	154.2	144.3	146.8
	74	120.7	137.2	135.6	124.5	129.6	161.0	169.8	168.2	161.0	148.2
	75	125.9	136.7	137.8	138.9	134.1	165.1	175.6	172.9	170.4	157.5
	76	120.4	133.0	133.5	133.2	130.5	142.2	145.0	141.8	143.9	137.6
	77	99.5	107.9	113.2	110.0	108.9	124.9	122.1	125.9	130.1	135.7
	78	107.8	113.3	116.1	111.9	109.3	127.5	129.2	137.6	130.5	132.4
	79	122.8	130.5	135.7	121.4	119.2	179.9	183.9	178.0	166.2	166.8
	80	110.4	121.4	124.4	124.3	119.3	142.6	145.4	148.9	150.7	141.3

Individual Food and Water Consumption

Males

Group	Animal Number	Food (g/wk)			Water (g/wk)		
		Week 11	Week 12	Week 13*	Week 11	Week 12	Week 13*
7	61	128.5	141.1	92.3	185.8	174.6	93.7
	62	121.4	123.7	78.0	162.0	150.7	66.9
	63	120.4	128.4	88.4	147.1	150.9	68.6
	64	122.8	129.2	85.5	164.5	158.5	63.0
	65	120.3	127.9	81.1	135.2	136.8	60.5
	66	126.9	131.1	81.9	157.4	166.0	91.0
	67	131.6	138.6	92.3	161.4	160.6	93.2
	68	128.9	129.0	87.4	147.7	151.9	74.2
	69	109.5	117.8	81.8	167.2	179.8	99.6
	70	121.3	122.2	83.0	144.0	148.9	75.1
8	71	122.9	137.8	91.7	140.7	144.0	67.1
	72	130.5	122.2	91.2	160.1	150.7	83.0
	73	121.6	135.7	91.4	143.3	140.2	58.3
	74	129.5	124.7	87.6	140.4	146.9	74.4
	75	145.7	134.1	92.4	149.5	152.9	55.0
	76	127.3	136.9	92.6	127.3	134.7	56.8
	77	111.1	113.5	82.3	130.9	135.8	50.0
	78	122.7	123.6	65.2	130.4	132.2	59.3
	79	114.6	122.1	75.7	161.7	153.0	66.5
	80	124.3	129.4	86.7	144.4	146.7	55.1

*Week 13 is only 5 days

APPENDIX B

BODY WEIGHTS

Weekly Body Weights (grams)/Females

Dose (mg tetryl/kg diet)	Animal Number	Weeks							
		1	2	3	4	5	6	7	8
3000	1	123.45	129.13	137.87	141.10	142.33	148.57	152.03	152.50
	2	125.75	131.00	139.13	142.63	146.57	151.33	151.93	154.03
	3	123.30	128.60	137.23	143.80	148.27	153.40	157.00	159.33
	4	124.50	132.30	143.23	146.67	151.17	155.73	154.97	159.00
	5	125.60	135.47	146.27	151.73	153.07	157.27	158.63	160.60
	6	126.80	137.13	146.50	149.80	152.23	156.17	156.63	157.77
	7	124.65	134.27	140.47	143.50	149.87	152.20	154.53	153.60
	8	124.55	131.33	139.47	144.93	148.20	152.93	157.57	160.07
	9	121.80	127.90	136.03	140.77	148.13	152.87	152.40	152.53
	10	118.30	124.77	133.20	138.97	141.40	145.97	148.80	150.60
1000	11	132.45	141.60	148.63	155.60	159.80	161.57	165.57	166.93
	12	129.10	136.70	142.87	148.47	152.73	156.67	161.07	162.57
	13	127.65	137.57	145.33	150.17	153.67	158.47	160.67	163.10
	14	127.45	134.83	141.83	148.23	152.73	157.10	158.67	160.80
	15	124.00	134.33	143.33	149.70	152.50	155.17	157.53	160.97
	16	125.45	133.90	142.27	147.83	151.77	153.23	158.37	161.87
	17	128.25	138.57	148.20	151.83	156.90	162.93	166.63	168.50
	18	123.75	132.47	140.33	145.63	149.30	152.00	154.37	155.17
	19	130.90	143.57	151.60	158.33	163.53	167.07	174.77	177.77
	20	116.60	126.57	134.80	137.87	141.13	145.80	149.53	151.43
200	21	129.05	139.37	147.43	152.33	155.47	160.50	163.63	165.80
	22	130.25	137.37	144.37	150.37	157.00	160.50	163.87	168.03
	23	131.50	140.17	149.70	155.57	158.80	165.07	170.63	173.00
	24	126.15	133.13	140.50	147.03	152.33	158.30	161.83	164.43
	25	123.85	131.73	139.00	143.30	146.63	150.90	155.50	157.33
	26	122.45	134.00	143.57	149.67	154.70	160.00	163.53	168.73
	27	128.45	138.10	147.87	155.03	160.77	169.40	174.17	176.83
	28	121.50	131.57	139.97	144.60	146.23	152.80	157.17	159.07
	29	124.50	135.40	145.40	150.87	158.37	165.07	168.77	173.17
	30	117.50	125.50	132.43	138.33	143.40	149.00	152.90	153.53
0	31	134.30	147.17	155.20	161.93	166.67	172.50	180.30	184.33
	32	132.30	142.13	150.23	156.47	160.03	165.17	169.40	171.57
	33	126.85	136.30	142.87	147.53	152.80	158.30	160.50	162.43
	34	125.00	134.43	143.17	148.53	152.47	157.73	162.73	164.57
	35	126.35	136.67	143.80	147.40	150.77	153.50	159.77	163.70
	36	125.50	135.40	142.20	146.67	150.30	156.23	160.37	161.70
	37	123.65	132.73	141.17	147.93	153.53	160.80	166.33	168.30
	38	124.25	134.27	143.57	150.63	156.43	161.47	168.37	171.17
	39	125.45	137.03	146.00	151.70	156.27	161.33	166.30	169.10
	40	120.80	133.53	142.60	146.27	149.53	152.07	155.97	161.60

Week 1 was only 6 days.

Weekly Body Weights (grams)/Females

Dose (mg tetryl/kg diet)	Animal Number	Weeks				
		9	10	11	12	13
3000	1	153.60	155.00	159.83	161.17	158.00
	2	159.40	163.37	163.87	162.97	163.77
	3	161.53	163.80	164.13	163.27	166.67
	4	161.23	164.77	164.00	163.87	164.77
	5	162.50	161.63	161.23	162.40	164.80
	6	160.97	163.30	166.00	167.10	168.90
	7	153.03	155.60	158.57	161.93	160.60
	8	162.73	164.03	162.83	162.53	165.43
	9	155.43	159.20	161.37	163.13	161.10
	10	153.57	155.97	157.63	161.73	161.57
1000	11	168.50	171.10	174.43	176.23	177.07
	12	164.93	167.13	171.70	175.23	175.40
	13	166.50	167.83	168.83	168.83	170.23
	14	165.90	168.27	168.33	170.60	170.37
	15	164.80	167.00	167.43	168.70	170.30
	16	163.20	165.20	166.07	168.10	169.43
	17	171.23	172.97	175.40	179.17	179.80
	18	158.50	162.67	161.97	163.23	164.63
	19	179.93	181.93	183.30	185.77	188.07
	20	154.37	156.67	156.47	156.90	158.23
200	21	168.13	170.07	173.37	174.00	176.33
	22	170.93	172.93	173.73	175.97	179.93
	23	176.47	178.87	179.43	180.73	180.60
	24	169.00	172.90	176.80	181.67	183.90
	25	159.67	160.83	159.17	160.20	161.20
	26	171.87	174.77	175.80	177.77	181.53
	27	180.43	182.30	184.57	185.33	185.27
	28	163.87	166.43	165.77	168.53	170.97
	29	175.77	181.43	183.50	185.53	187.80
	30	156.40	159.50	160.87	161.73	164.33
0	31	187.77	188.00	189.23	192.70	194.17
	32	176.23	180.80	181.70	184.07	185.30
	33	167.13	169.37	171.97	174.10	174.00
	34	168.53	171.90	172.00	172.47	173.90
	35	165.73	166.70	168.20	169.00	172.80
	36	165.33	167.00	169.30	170.47	171.00
	37	170.60	171.30	175.00	179.47	184.40
	38	173.30	177.30	177.57	180.33	184.50
	39	171.97	175.63	177.97	181.60	182.03
	40	167.07	170.10	172.20	175.53	178.27

Weekly Body Weights (grams)/Males

Dose (mg tetryl/kg diet)	Animal Number	Weeks							
		1	2	3	4	5	6	7	8
3000	41	177.95	189.07	207.87	220.87	233.70	247.93	259.30	264.87
	42	175.85	190.77	214.30	233.37	248.23	260.37	270.97	274.37
	43	171.65	185.97	207.07	223.97	235.40	248.47	262.70	272.50
	44	171.90	186.97	209.77	225.90	238.90	250.50	261.97	269.17
	45	164.00	173.03	191.57	204.70	216.40	229.37	243.10	252.53
	46	168.55	187.73	212.73	232.47	249.37	264.60	279.40	291.73
	47	166.40	179.70	200.33	217.90	234.30	249.57	260.80	268.43
	48	164.70	178.80	201.83	219.63	237.43	252.27	264.70	276.43
	49	155.30	167.07	187.40	202.50	218.10	231.70	243.47	250.23
	50	151.10	163.77	185.90	200.30	212.53	227.27	237.90	247.43
1000	51	179.45	198.40	221.63	239.70	254.87	270.90	280.67	288.23
	52	180.70	200.53	222.37	239.00	254.53	269.67	281.47	288.90
	53	179.55	199.33	220.83	234.90	249.20	263.73	272.27	277.33
	54	175.50	194.93	215.53	229.03	243.20	258.93	268.40	275.47
	55	173.15	191.30	213.47	229.47	242.33	257.43	270.93	276.03
	56	166.20	181.13	194.43	204.57	215.63	228.90	246.07	255.30
	57	164.85	185.03	209.23	226.87	242.03	257.10	269.43	278.23
	58	167.80	191.27	217.83	238.30	255.47	272.33	285.43	295.20
	59	156.70	176.63	203.70	222.73	239.27	254.20	265.40	276.57
	60	162.95	182.67	202.30	219.60	234.67	243.23	252.93	261.57
200	61	198.50	220.20	244.23	257.60	269.17	285.97	301.47	307.77
	62	180.35	201.03	223.70	237.47	251.67	266.47	281.50	288.57
	63	173.85	191.70	214.57	229.57	243.37	258.60	270.00	280.63
	64	174.80	195.57	218.80	232.63	243.17	257.50	274.57	284.87
	65	178.30	197.37	218.30	235.47	252.47	269.00	282.30	291.30
	66	173.10	194.57	219.37	231.30	240.70	254.90	270.13	280.27
	67	170.15	191.70	214.40	232.83	249.80	267.53	282.33	292.50
	68	170.20	192.07	213.93	227.80	238.83	253.97	268.90	278.27
	69	164.60	181.93	202.87	216.17	227.63	240.60	248.37	256.70
	70	162.70	183.90	204.03	218.20	231.00	244.73	259.47	270.33
0	71	176.75	194.17	212.80	224.87	237.00	251.57	266.53	274.77
	72	179.25	199.33	219.37	235.27	252.13	269.30	285.13	296.27
	73	180.05	199.57	216.50	227.67	240.80	257.87	274.10	281.70
	74	178.75	202.27	227.37	241.53	254.83	269.43	282.13	292.17
	75	171.40	192.53	216.53	233.73	248.17	265.00	281.50	294.70
	76	172.40	194.33	222.40	240.43	253.43	266.80	280.50	290.93
	77	162.90	181.57	198.03	207.57	214.53	226.47	236.00	245.97
	78	173.15	193.03	210.67	221.37	229.97	241.83	255.80	264.50
	79	170.50	189.87	209.23	226.27	240.27	253.77	270.47	278.53
	80	166.50	186.40	206.73	222.43	230.30	241.40	254.13	266.80

Week 1 was only 6 days.

Weekly Body Weights (grams)/Males

Dose (mg tetryl/kg diet)	Animal Number	Weeks				
		9	10	11	12	13
3000	41	272.13	278.97	282.50	287.03	289.70
	42	276.83	286.50	292.83	301.27	307.20
	43	278.27	281.90	288.10	295.70	299.70
	44	277.87	281.53	284.63	290.23	290.10
	45	258.97	268.70	272.87	279.53	284.20
	46	299.67	309.73	318.37	324.87	331.60
	47	277.03	283.87	290.20	297.93	302.20
	48	282.80	291.53	300.87	307.57	313.50
	49	254.00	261.00	268.90	276.13	281.40
	50	251.43	258.77	262.67	266.80	271.20
1000	51	293.00	299.50	306.70	316.17	321.50
	52	295.77	306.50	315.93	322.83	329.30
	53	284.67	292.47	299.57	309.33	313.80
	54	284.07	294.20	300.60	307.77	312.50
	55	280.00	287.03	292.30	297.83	300.90
	56	266.33	274.47	285.03	291.50	294.70
	57	286.63	295.23	302.70	311.40	314.40
	58	304.00	313.80	325.73	331.10	337.30
	59	285.97	293.83	300.10	307.67	311.60
	60	272.10	279.97	285.30	292.00	299.00
200	61	317.77	329.47	336.83	341.30	342.90
	62	295.23	303.90	312.87	317.77	320.50
	63	289.90	297.03	305.33	313.50	315.30
	64	289.60	299.93	309.83	312.13	315.00
	65	298.53	307.73	311.70	316.73	320.00
	66	288.93	296.60	303.27	312.53	318.80
	67	302.37	314.50	323.87	332.60	338.20
	68	285.83	293.23	303.53	309.23	312.50
	69	266.63	272.60	276.83	286.03	291.50
	70	278.60	286.47	293.87	302.87	309.40
0	71	281.93	293.07	300.40	308.47	313.40
	72	304.10	313.53	321.77	329.20	333.80
	73	288.63	298.53	306.37	315.10	327.10
	74	302.57	307.87	313.67	322.30	332.10
	75	307.37	317.93	327.63	336.40	344.20
	76	300.03	307.37	316.10	324.23	328.50
	77	255.27	263.97	272.47	281.60	288.00
	78	276.30	286.40	292.17	301.07	306.20
	79	285.77	291.97	298.73	306.87	311.00
	80	278.37	285.83	293.57	303.60	308.20

APPENDIX C

ORGAN WEIGHTS

INDIVIDUAL ORGAN WEIGHTS

GROUP NUMBER		BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
1	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	153.33	1.311	0.956	5.130	0.855	0.623	3.347
	S.E.M.	1.00	0.014	0.026	0.033	0.010	0.017	0.031
2	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	163.70	1.260	0.936	4.972	0.769	0.572	3.036
	S.E.M.	2.49	0.030	0.019	0.112	0.009	0.009	0.041
3	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	168.44	1.295	0.961	4.840	0.769	0.571	2.873
	S.E.M.	2.52	0.025	0.039	0.099	0.012	0.022	0.037
4	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	171.55	1.250	1.015	4.731	0.728	0.592	2.761
	S.E.M.	2.13	0.018	0.028	0.048	0.006	0.017	0.039
5	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	279.95	2.401	1.411	11.033	0.858	0.505	3.938
	S.E.M.	4.71	0.052	0.044	0.248	0.009	0.014	0.029
6	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	297.37	2.396	1.424	10.073	0.806	0.478	3.385
	S.E.M.	3.89	0.102	0.066	0.226	0.036	0.018	0.040
7	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	305.04	2.291	1.470	9.347	0.751	0.482	3.062
	S.E.M.	4.12	0.047	0.078	0.224	0.009	0.025	0.046
8	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	304.19	2.203	1.422	9.347	0.724	0.468	3.068
	S.E.M.	4.78	0.049	0.039	0.256	0.012	0.012	0.044

INDIVIDUAL ORGAN WEIGHTS

GROUP NUMBER		BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
1	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	153.33	0.654	1.686	0.465	0.427	1.100	0.303
	S.E.M.	1.00	0.024	0.014	0.009	0.016	0.013	0.006
2	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	163.70	0.640	1.717	0.438	0.390	1.052	0.267
	S.E.M.	2.49	0.021	0.018	0.012	0.010	0.022	0.004
3	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	168.44	0.649	1.773	0.417	0.385	1.056	0.247
	S.E.M.	2.52	0.021	0.046	0.012	0.009	0.036	0.004
4	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	171.55	0.686	1.826	0.438	0.400	1.066	0.255
	S.E.M.	2.13	0.017	0.022	0.011	0.008	0.018	0.005
5	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	279.95	0.929	1.833	0.707	0.332	0.656	0.253
	S.E.M.	4.71	0.019	0.015	0.015	0.005	0.010	0.004
6	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	297.37	0.963	1.896	0.625	0.324	0.638	0.210
	S.E.M.	3.89	0.019	0.026	0.011	0.006	0.012	0.004
7	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	305.04	1.052	1.915	0.613	0.345	0.628	0.201
	S.E.M.	4.12	0.034	0.017	0.011	0.010	0.007	0.003
8	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	304.19	0.995	1.899	0.611	0.327	0.626	0.201
	S.E.M.	4.78	0.024	0.015	0.011	0.008	0.010	0.004

INDIVIDUAL ORGAN WEIGHTS

GROUP NUMBER		BODY WEIGHT	ADRENAL WEIGHT	THYMUS WEIGHT	OVARIES/ TESTES		% ADRENAL	% THYMUS	% OVARIES/ TESTES
					WEIGHT	% WEIGHT			
1	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	153.33	0.070	0.193	0.130	0.045	0.126	0.085	
	S.E.M.	1.00	0.003	0.007	0.005	0.002	0.005	0.003	
2	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	163.70	0.069	0.218	0.213	0.042	0.133	0.129	
	S.E.M.	2.49	0.004	0.009	0.087	0.003	0.005	0.052	
3	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	168.44	0.083	0.218	0.140	0.049	0.129	0.083	
	S.E.M.	2.52	0.006	0.010	0.008	0.004	0.006	0.004	
4	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	171.55	0.087	0.245	0.165	0.051	0.143	0.096	
	S.E.M.	2.13	0.005	0.015	0.020	0.003	0.009	0.011	
5	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	279.95	0.074	0.249	4.816	0.027	0.089	1.722	
	S.E.M.	4.71	0.005	0.016	0.166	0.002	0.005	0.055	
6	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	297.37	0.068	0.265	4.978	0.023	0.089	1.671	
	S.E.M.	3.89	0.004	0.022	0.237	0.001	0.007	0.070	
7	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	305.04	0.069	0.255	5.366	0.023	0.084	1.756	
	S.E.M.	4.12	0.002	0.013	0.278	0.001	0.004	0.082	
8	N	10.00	10.000	10.000	10.000	10.000	10.000	10.000	10.000
	MEAN	304.19	0.072	0.287	5.082	0.024	0.094	1.672	
	S.E.M.	4.78	0.005	0.022	0.288	0.002	0.006	0.094	

INDIVIDUAL ORGAN WEIGHTS

GP-ANI NUMBER	BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
1 1	148.95	1.313	0.862	5.002	0.882	0.579	3.358
1 2	153.58	1.280	1.064	5.133	0.833	0.693	3.342
1 3	156.81	1.332	0.997	5.161	0.849	0.636	3.291
1 4	155.47	1.299	0.944	5.122	0.836	0.607	3.295
1 5	156.70	1.389	1.039	4.928	0.886	0.663	3.145
1 6	157.07	1.285	0.965	5.229	0.818	0.614	3.329
1 7	149.25	1.309	1.054	5.183	0.877	0.706	3.473
1 8	153.35	1.347	0.832	5.264	0.878	0.543	3.433
1 9	149.98	1.334	0.926	5.210	0.889	0.617	3.474
1 10	152.09	1.225	0.873	5.065	0.805	0.574	3.330
2 11	168.22	1.303	0.987	5.605	0.775	0.587	3.332
2 12	166.63	1.271	0.954	4.981	0.763	0.573	2.989
2 13	162.12	1.231	0.909	4.829	0.759	0.561	2.979
2 14	159.27	1.280	0.980	4.941	0.804	0.615	3.102
2 15	165.27	1.303	0.955	5.101	0.788	0.578	3.086
2 16	161.13	1.163	0.934	4.601	0.722	0.580	2.855
2 17	168.25	1.326	0.989	4.901	0.788	0.588	2.913
2 18	156.99	1.164	0.928	4.685	0.741	0.591	2.984
2 19	179.24	1.438	0.940	5.513	0.802	0.524	3.076
2 20	149.83	1.119	0.779	4.562	0.747	0.520	3.045
3 21	168.04	1.318	0.791	4.727	0.784	0.471	2.813
3 22	168.32	1.333	1.214	4.687	0.792	0.721	2.785
3 23	171.62	1.207	1.019	5.171	0.703	0.594	3.013
3 24	173.76	1.368	0.981	5.035	0.787	0.565	2.898
3 25	154.01	1.182	0.817	4.383	0.767	0.530	2.846
3 26	172.60	1.382	1.028	4.955	0.801	0.596	2.871
3 27	178.17	1.290	0.916	4.795	0.724	0.514	2.691
3 28	159.54	1.314	0.850	4.781	0.824	0.533	2.997
3 29	177.34	1.383	0.976	5.407	0.780	0.550	3.049
3 30	161.04	1.175	1.017	4.459	0.730	0.632	2.769
4 31	185.80	1.391	1.127	4.732	0.749	0.607	2.547
4 32	176.08	1.282	1.060	4.956	0.728	0.602	2.815
4 33	168.91	1.234	0.941	4.886	0.731	0.557	2.893
4 34	164.16	1.239	0.998	4.486	0.755	0.608	2.733
4 35	163.46	1.186	1.059	4.741	0.726	0.648	2.900
4 36	166.38	1.234	1.132	4.653	0.742	0.680	2.797
4 37	174.28	1.239	0.934	4.704	0.711	0.536	2.699
4 38	175.21	1.241	1.080	4.716	0.708	0.616	2.692
4 39	172.71	1.195	0.871	4.534	0.692	0.504	2.625
4 40	168.54	1.254	0.943	4.899	0.744	0.560	2.907

INDIVIDUAL ORGAN WEIGHTS

GP-ANI NUMBER		BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
1	1	148.95	0.695	1.686	0.409	0.467	1.132	0.275
1	2	153.58	0.574	1.777	0.473	0.374	1.157	0.308
1	3	156.81	0.625	1.656	0.507	0.399	1.056	0.323
1	4	155.47	0.656	1.666	0.452	0.422	1.072	0.291
1	5	156.70	0.677	1.608	0.445	0.432	1.026	0.284
1	6	157.07	0.634	1.719	0.469	0.404	1.094	0.299
1	7	149.25	0.623	1.673	0.461	0.417	1.121	0.309
1	8	153.35	0.840	1.680	0.514	0.548	1.096	0.335
1	9	149.98	0.567	1.724	0.458	0.378	1.149	0.305
1	10	152.09	0.651	1.666	0.462	0.428	1.095	0.304
2	11	168.22	0.610	1.755	0.467	0.363	1.043	0.278
2	12	166.63	0.791	1.684	0.417	0.475	1.011	0.250
2	13	162.12	0.628	1.709	0.431	0.387	1.054	0.266
2	14	159.27	0.601	1.781	0.423	0.377	1.118	0.266
2	15	165.27	0.677	1.759	0.453	0.410	1.064	0.274
2	16	161.13	0.620	1.725	0.405	0.385	1.071	0.251
2	17	168.25	0.654	1.736	0.455	0.389	1.032	0.270
2	18	156.99	0.583	1.750	0.436	0.371	1.115	0.278
2	19	179.24	0.681	1.584	0.517	0.380	0.884	0.288
2	20	149.83	0.552	1.688	0.376	0.368	1.127	0.251
3	21	168.04	0.606	1.447	0.389	0.361	0.861	0.231
3	22	168.32	0.710	1.800	0.439	0.422	1.069	0.261
3	23	171.62	0.660	1.665	0.438	0.385	0.970	0.255
3	24	173.76	0.648	1.752	0.405	0.373	1.008	0.233
3	25	154.01	0.579	1.995	0.359	0.376	1.295	0.233
3	26	172.60	0.755	1.741	0.410	0.437	1.009	0.238
3	27	178.17	0.651	1.906	0.447	0.365	1.070	0.251
3	28	159.54	0.588	1.824	0.393	0.369	1.143	0.246
3	29	177.34	0.728	1.825	0.489	0.411	1.029	0.276
3	30	161.04	0.567	1.772	0.401	0.352	1.100	0.249
4	31	185.80	0.770	1.906	0.522	0.414	1.026	0.281
4	32	176.08	0.744	1.744	0.444	0.423	0.990	0.252
4	33	168.91	0.653	1.945	0.434	0.387	1.152	0.257
4	34	164.16	0.665	1.867	0.452	0.405	1.137	0.275
4	35	163.46	0.646	1.794	0.426	0.395	1.098	0.261
4	36	166.38	0.655	1.801	0.433	0.394	1.082	0.260
4	37	174.28	0.625	1.774	0.406	0.359	1.018	0.233
4	38	175.21	0.708	1.827	0.455	0.404	1.043	0.260
4	39	172.71	0.634	1.726	0.391	0.367	0.999	0.226
4	40	168.54	0.755	1.873	0.419	0.448	1.111	0.249

INDIVIDUAL ORGAN WEIGHTS

GP-ANI NUMBER		BODY WEIGHT	ADRENAL WEIGHT	THYMUS WEIGHT	OVARIES WEIGHT	% ADRENAL	% THYMUS	% OVARIES
1	1	148.95	0.080	0.232	0.133	0.054	0.156	0.089
1	2	153.58	0.075	0.154	0.128	0.049	0.100	0.083
1	3	156.81	0.058	0.207	0.129	0.037	0.132	0.082
1	4	155.47	0.080	0.187	0.120	0.051	0.120	0.077
1	5	156.70	0.060	0.174	0.126	0.038	0.111	0.080
1	6	157.07	0.080	0.196	0.134	0.051	0.125	0.085
1	7	149.25	0.065	0.183	0.122	0.044	0.123	0.082
1	8	153.35	0.074	0.204	0.168	0.048	0.133	0.110
1	9	149.98	0.069	0.194	0.122	0.046	0.129	0.081
1	10	152.09	0.056	0.200	0.118	0.037	0.132	0.078
2	11	168.22	0.063	0.234	0.147	0.037	0.139	0.087
2	12	166.63	0.061	0.220	0.150	0.037	0.132	0.090
2	13	162.12	0.071	0.178	0.135	0.044	0.110	0.083
2	14	159.27	0.086	0.216	0.128	0.054	0.136	0.080
2	15	165.27	0.065	0.216	0.990	0.039	0.131	0.599
2	16	161.13	0.066	0.203	0.109	0.041	0.126	0.068
2	17	168.25	0.047	0.282	0.140	0.028	0.168	0.083
2	18	156.99	0.066	0.219	0.116	0.042	0.139	0.074
2	19	179.24	0.096	0.230	0.130	0.054	0.128	0.073
2	20	149.83	0.071	0.184	0.081	0.047	0.123	0.054
3	21	168.04	0.101	0.269	0.161	0.060	0.160	0.096
3	22	168.32	0.053	0.168	0.125	0.031	0.100	0.074
3	23	171.62	0.065	0.183	0.132	0.038	0.107	0.077
3	24	173.76	0.078	0.238	0.173	0.045	0.137	0.100
3	25	154.01	0.107	0.213	0.135	0.069	0.138	0.088
3	26	172.60	0.086	0.243	0.144	0.050	0.141	0.083
3	27	178.17	0.096	0.211	0.146	0.054	0.118	0.082
3	28	159.54	0.079	0.229	0.088	0.050	0.144	0.055
3	29	177.34	0.099	0.231	0.175	0.056	0.130	0.099
3	30	161.04	0.062	0.190	0.125	0.038	0.118	0.078
4	31	185.80	0.080	0.211	0.196	0.043	0.114	0.105
4	32	176.08	0.080	0.258	0.332	0.045	0.147	0.189
4	33	168.91	0.119	0.279	0.161	0.070	0.165	0.095
4	34	164.16	0.094	0.280	0.147	0.057	0.171	0.090
4	35	163.46	0.082	0.243	0.147	0.050	0.149	0.090
4	36	166.38	0.075	0.180	0.120	0.045	0.108	0.072
4	37	174.28	0.097	0.335	0.163	0.056	0.192	0.094
4	38	175.21	0.072	0.206	0.127	0.041	0.118	0.072
4	39	172.71	0.078	0.207	0.128	0.045	0.120	0.074
4	40	168.54	0.097	0.249	0.129	0.058	0.148	0.077

INDIVIDUAL ORGAN WEIGHTS

GP-ANI NUMBER		BODY WEIGHT	KIDNEY WEIGHT	LUNGS WEIGHT	LIVER WEIGHT	% KIDNEY	% LUNGS	% LIVER
5	41	275.59	2.307	1.386	10.529	0.837	0.503	3.821
5	42	287.56	2.420	1.507	11.186	0.842	0.524	3.890
5	43	282.44	2.307	1.303	10.987	0.817	0.461	3.890
5	44	276.40	2.504	1.292	11.062	0.906	0.467	4.002
5	45	273.40	2.438	1.238	10.920	0.892	0.453	3.994
5	46	307.45	2.701	1.386	12.732	0.879	0.451	4.141
5	47	281.32	2.399	1.641	11.029	0.853	0.583	3.920
5	48	296.06	2.561	1.629	11.741	0.865	0.550	3.966
5	49	262.23	2.144	1.350	10.117	0.818	0.515	3.858
5	50	257.02	2.231	1.382	10.025	0.868	0.538	3.900
6	51	302.87	2.256	1.451	10.058	0.745	0.479	3.321
6	52	311.28	2.503	1.677	10.366	0.804	0.539	3.330
6	53	298.84	2.458	1.769	10.131	0.823	0.592	3.390
6	54	294.26	2.228	1.190	9.501	0.757	0.404	3.229
6	55	287.16	3.217	1.369	9.747	1.120	0.477	3.394
6	56	284.23	2.188	1.183	9.441	0.770	0.416	3.322
6	57	294.41	2.233	1.491	10.277	0.758	0.506	3.491
6	58	321.50	2.523	1.595	11.848	0.785	0.496	3.685
6	59	297.76	2.241	1.299	9.972	0.753	0.436	3.349
6	60	281.36	2.111	1.220	9.388	0.750	0.434	3.337
7	61	326.21	2.514	1.542	10.420	0.771	0.473	3.194
7	62	304.62	2.203	1.346	9.336	0.723	0.442	3.065
7	63	304.08	2.312	1.086	9.682	0.760	0.357	3.184
7	64	302.80	2.333	1.718	9.710	0.770	0.567	3.207
7	65	303.50	2.296	1.385	9.214	0.757	0.456	3.036
7	66	297.89	2.185	1.244	8.847	0.733	0.418	2.970
7	67	326.81	2.484	1.912	9.789	0.760	0.585	2.995
7	68	303.23	2.132	1.344	9.853	0.703	0.443	3.249
7	69	282.60	2.053	1.679	7.944	0.726	0.594	2.811
7	70	298.64	2.399	1.439	8.677	0.803	0.482	2.906
8	71	304.09	2.266	1.490	9.435	0.745	0.490	3.103
8	72	322.17	2.368	1.354	10.695	0.735	0.420	3.320
8	73	307.77	2.105	1.407	9.859	0.684	0.457	3.203
8	74	312.59	2.416	1.428	9.897	0.773	0.457	3.166
8	75	325.51	2.196	1.479	9.894	0.675	0.454	3.040
8	76	313.40	2.251	1.594	9.668	0.718	0.509	3.085
8	77	279.40	1.993	1.335	8.417	0.713	0.478	3.013
8	78	285.36	1.943	1.354	8.198	0.681	0.474	2.873
8	79	294.28	2.177	1.190	8.491	0.740	0.404	2.885
8	80	297.32	2.317	1.586	8.913	0.779	0.533	2.998

INDIVIDUAL ORGAN WEIGHTS

GP-ANI NUMBER		BODY WEIGHT	HEART WEIGHT	BRAIN WEIGHT	SPLEEN WEIGHT	% HEART	% BRAIN	% SPLEEN
5	41	275.59	0.939	1.867	0.754	0.341	0.677	0.274
5	42	287.56	0.892	1.825	0.696	0.310	0.635	0.242
5	43	282.44	0.955	1.845	0.748	0.338	0.653	0.265
5	44	276.40	0.929	1.832	0.719	0.336	0.663	0.260
5	45	273.40	0.907	1.831	0.642	0.332	0.670	0.235
5	46	307.45	0.981	1.930	0.722	0.319	0.628	0.235
5	47	281.32	1.032	1.741	0.708	0.367	0.619	0.252
5	48	296.06	0.964	1.810	0.769	0.326	0.611	0.260
5	49	262.23	0.833	1.837	0.685	0.318	0.701	0.261
5	50	257.02	0.855	1.814	0.623	0.333	0.706	0.242
6	51	302.87	1.040	1.980	0.576	0.343	0.654	0.190
6	52	311.28	1.015	1.925	0.660	0.326	0.618	0.212
6	53	298.84	1.033	1.888	0.642	0.346	0.632	0.215
6	54	294.26	0.927	1.956	0.598	0.315	0.665	0.203
6	55	287.16	0.983	1.855	0.611	0.342	0.646	0.213
6	56	284.23	0.967	1.907	0.623	0.340	0.671	0.219
6	57	294.41	0.930	1.893	0.567	0.316	0.643	0.193
6	58	321.50	0.973	1.912	0.661	0.303	0.595	0.206
6	59	297.76	0.919	1.686	0.665	0.309	0.566	0.223
6	60	281.36	0.841	1.954	0.644	0.299	0.694	0.229
7	61	326.21	1.075	1.924	0.607	0.330	0.590	0.186
7	62	304.62	0.981	1.925	0.590	0.322	0.632	0.194
7	63	304.08	0.966	1.897	0.560	0.318	0.624	0.184
7	64	302.80	1.105	1.893	0.629	0.365	0.625	0.208
7	65	303.50	1.186	1.828	0.638	0.391	0.602	0.210
7	66	297.89	1.071	1.941	0.584	0.360	0.652	0.196
7	67	326.81	1.256	2.021	0.676	0.384	0.618	0.207
7	68	303.23	0.953	1.881	0.651	0.314	0.620	0.215
7	69	282.60	1.010	1.872	0.591	0.357	0.662	0.209
7	70	298.64	0.918	1.965	0.606	0.307	0.658	0.203
8	71	304.09	1.079	1.834	0.582	0.355	0.603	0.191
8	72	322.17	0.978	1.974	0.648	0.304	0.613	0.201
8	73	307.77	0.907	1.944	0.598	0.295	0.632	0.194
8	74	312.59	0.970	1.947	0.617	0.310	0.623	0.197
8	75	325.51	0.971	1.864	0.628	0.298	0.573	0.193
8	76	313.40	1.109	1.874	0.600	0.354	0.598	0.191
8	77	279.40	0.880	1.917	0.550	0.315	0.686	0.197
8	78	285.36	0.963	1.852	0.657	0.337	0.649	0.230
8	79	294.28	1.001	1.927	0.577	0.340	0.655	0.196
8	80	297.32	1.089	1.860	0.649	0.366	0.626	0.218

INDIVIDUAL ORGAN WEIGHTS

GP-ANI NUMBER		BODY WEIGHT	ADRENAL WEIGHT	THYMUS WEIGHT	TESTES WEIGHT	% ADRENAL	% THYMUS	% TESTES
5	41	275.59	0.072	0.297	4.600	0.026	0.108	1.669
5	42	287.56	0.051	0.180	4.652	0.018	0.063	1.618
5	43	282.44	0.076	0.303	4.607	0.027	0.107	1.631
5	44	276.40	0.111	0.246	4.568	0.040	0.089	1.653
5	45	273.40	0.077	0.188	4.565	0.028	0.069	1.670
5	46	307.45	0.087	0.342	4.629	0.028	0.111	1.506
5	47	281.32	0.070	0.234	5.843	0.025	0.083	2.077
5	48	296.06	0.061	0.234	5.719	0.021	0.079	1.932
5	49	262.23	0.064	0.236	4.259	0.024	0.090	1.624
5	50	257.02	0.072	0.234	4.720	0.028	0.091	1.836
6	51	302.87	0.090	0.368	4.834	0.030	0.122	1.596
6	52	311.28	0.064	0.178	6.354	0.021	0.057	2.041
6	53	298.84	0.056	0.183	6.329	0.019	0.061	2.118
6	54	294.26	0.050	0.211	4.786	0.017	0.072	1.626
6	55	287.16	0.066	0.238	4.680	0.023	0.083	1.630
6	56	284.23	0.070	0.254	4.276	0.025	0.089	1.504
6	57	294.41	0.059	0.318	4.675	0.020	0.108	1.588
6	58	321.50	0.065	0.330	5.000	0.020	0.103	1.555
6	59	297.76	0.094	0.337	4.450	0.032	0.113	1.494
6	60	281.36	0.069	0.232	4.391	0.025	0.082	1.561
7	61	326.21	0.075	0.220	6.540	0.023	0.067	2.005
7	62	304.62	0.073	0.250	4.767	0.024	0.082	1.565
7	63	304.08	0.060	0.215	4.323	0.020	0.071	1.422
7	64	302.80	0.066	0.229	5.870	0.022	0.076	1.939
7	65	303.50	0.064	0.249	6.102	0.021	0.082	2.011
7	66	297.89	0.071	0.233	4.410	0.024	0.078	1.480
7	67	326.81	0.081	0.313	6.527	0.025	0.096	1.997
7	68	303.23	0.056	0.348	4.745	0.018	0.115	1.565
7	69	282.60	0.070	0.238	5.745	0.025	0.084	2.033
7	70	298.64	0.072	0.254	4.626	0.024	0.085	1.549
8	71	304.09	0.063	0.231	6.542	0.021	0.076	2.151
8	72	322.17	0.091	0.228	4.589	0.028	0.071	1.424
8	73	307.77	0.055	0.319	4.390	0.018	0.104	1.426
8	74	312.59	0.099	0.304	4.860	0.032	0.097	1.555
8	75	325.51	0.073	0.385	4.624	0.022	0.118	1.421
8	76	313.40	0.078	0.410	6.584	0.025	0.131	2.101
8	77	279.40	0.062	0.253	4.516	0.022	0.091	1.616
8	78	285.36	0.086	0.289	4.676	0.030	0.101	1.639
8	79	294.28	0.057	0.202	4.125	0.019	0.069	1.402
8	80	297.32	0.058	0.252	5.911	0.020	0.085	1.988

APPENDIX D

HEMATOLOGY DATA

Hematology Data/Females
45 Days

DOSE GROUPS (mg tetryl/kg) diet	ANIMAL #	RBC	HGB	HCT	WBC		
		COUNT mill/ cu mm			PLATELETS thsn/ cu mm	COUNT thsn/ cu mm	METHB %
3000	401	7.83	14.7	43.2	864	3.7	2.3
	402	7.58	13.4	41.9	903	4.9	1.3
	403	7.91	14.9	43.0	765	5.0	1.9
	404	7.55	13.9	40.9	721	4.6	2.0
	405	8.16	14.9	45.4	729	5.7	2.3
1000	406	7.96	14.2	44.1	500	5.0	1.2
	407	8.25	15.3	46.6	772	5.0	1.1
	408	7.79	14.5	42.1	806	4.8	1.5
	409	7.84	14.7	43.9	719	4.3	0.9
	410	7.88	14.6	42.2	786	4.4	0.8
200	411	7.84	14.7	41.9	722	4.1	0.4
	412	8.05	15.4	43.3	865	4.2	1.2
	413	7.93	14.8	41.6	816	3.0	0.9
	414	7.87	14.5	41.6	710	5.5	1.1
	415	8.24	15.4	43.7	779	3.4	0.9
0	416	7.96	15.5	41.9	768	3.4	0.1
	417	8.01	15.5	42.6	725	4.6	0.1
	418	8.12	15.6	43.5	819	4.1	0.5
	419	8.17	15.6	43.5	718	4.2	0.6
	420	8.49	16.1	47.1	863	4.6	0.1

Hematology Data/Females
45 Days

DOSE GROUPS (mg tetryl/kg) diet	ANIMAL #	cumi cr	picogm	g/dl	NEUTRO-	LYMPHO-	HEINZ	RETIC
					PHILS	CYTES	BODIES	
3000	401	55.1	18.7	34.0	12.6	83.2	0.0	4.4
	402	55.2	17.7	32.0	18.3	78.2	0.0	3.3
	403	54.4	18.8	34.5	13.3	84.3	0.0	3.4
	404	54.2	18.5	34.1	10.2	87.2	0.0	3.6
	405	55.6	18.2	32.7	10.0	85.5	0.0	3.7
1000	406	55.4	17.8	32.1	8.8	88.3	0.0	2.3
	407	56.5	18.5	32.8	14.2	81.7	0.0	2.5
	408	54.0	18.7	34.5	20.8	75.3	0.0	2.3
	409	56.0	18.8	33.6	18.1	77.5	0.0	2.3
	410	53.6	18.5	34.5	15.3	80.5	0.0	2.2
200	411	53.5	18.7	35.0	18.7	77.4	0.0	1.8
	412	53.7	19.1	35.5	26.5	69.4	0.0	1.9
	413	52.5	18.7	35.6	19.9	75.3	0.0	1.9
	414	52.8	18.5	35.0	17.7	78.9	0.0	1.7
	415	53.1	18.7	35.2	13.6	81.5	0.0	2.4
0	416	52.6	19.5	37.1	17.1	79.1	0.0	1.8
	417	53.2	19.3	36.3	19.1	77.6	0.0	2.0
	418	53.6	19.2	35.8	21.9	74.2	0.0	2.1
	419	53.2	19.0	35.8	21.9	75.0	0.0	1.8
	420	55.4	18.9	34.1	28.6	65.5	0.0	2.4

Hematology Data/Males
45 Days

DOSE GROUPS (mg tetryl/kg) diet	ANIMAL #	RBC			WBC		
		COUNT mill/ cu mm	HGB g/dl	HCT %	PLATELETS thsn/ cu mm	COUNT thsn/ cu mm	METHB %
3000	421	8.41	14.0	43.4	1042	4.6	2.8
	422	8.63	14.4	43.4	893	4.2	2.7
	423	8.25	13.6	42.2	914	3.8	2.3
	424	8.77	14.8	44.2	1006	5.0	2.7
	425	8.46	13.8	42.5	876	2.9	1.7
1000	426	8.70	15.1	43.8	873	3.0	1.4
	427	8.46	14.3	42.2	782	3.6	1.6
	428	8.77	15.3	44.9	844	5.1	1.6
	429	8.85	15.2	45.2	849	4.8	0.8
	430	8.76	14.6	43.6	873	4.5	1.4
200	431	8.70	14.8	43.9	805	3.3	0.6
	432	8.50	14.4	43.2	815	4.2	1.4
	433	9.00	15.9	46.0	781	4.9	1.1
	434	8.89	15.6	45.4	732	4.2	0.2
	435	9.28	16.3	47.5	812	4.4	1.1
0	436	8.51	15.0	43.5	678	4.1	0.1
	437	8.58	15.5	44.9	726	4.5	0.8
	438	8.63	15.4	44.7	828	5.4	0.7
	439	8.76	15.5	45.2	571	4.9	0.3
	440	8.80	15.8	46.2	700	4.0	0.2

Hematology Data/Males
45 Days

DOSE GROUPS	ANIMAL	MCV	MCH	MCHC	NEUTRO- PHILS	LYMPHO- CYTES	HEINZ BODIES	HEINZ RETIC
(mg tetryl/kg) diet	#	cumicr	picogr	g/dl	%	%	%	%
3000	421	51.6	16.6	32.3	16.8	79.8	0.0	4.4
	422	50.4	16.6	33.0	18.8	78.2	0.0	4.1
	423	51.2	16.4	32.1	15.7	80.6	0.0	4.1
	424	50.4	16.9	33.5	18.7	78.4	0.0	4.2
	425	50.2	16.3	32.4	24.7	72.2	0.0	4.0
1000	426	50.3	17.3	34.4	19.7	76.3	0.0	2.5
	427	49.9	16.9	33.9	24.9	71.7	0.0	3.1
	428	51.2	17.4	34.0	15.0	82.0	0.0	2.8
	429	51.1	17.1	33.5	18.8	77.7	0.0	3.1
	430	49.8	16.7	33.4	21.0	76.3	0.0	2.7
200	431	50.5	17.0	33.7	21.5	75.9	0.0	2.4
	432	50.9	16.9	33.3	23.8	72.4	0.0	2.6
	433	51.1	17.7	34.6	20.6	76.1	0.0	2.5
	434	51.1	17.5	34.3	18.7	78.3	0.0	2.0
	435	51.2	17.6	34.4	17.4	79.9	0.0	1.8
0	436	51.2	17.6	34.4	26.1	71.4	0.0	2.9
	437	52.3	18.1	34.6	22.2	75.4	0.0	2.5
	438	51.8	17.8	34.5	16.0	80.9	0.0	2.3
	439	51.6	17.7	34.3	14.8	82.5	0.0	2.2
	440	52.5	17.9	34.1	16.2	80.5	0.0	2.2

**Hematology Data/Females
90 Days**

DOSE GROUPS (mg tetryl/kg) diet	ANIMAL #	RBC			WBC		
		COUNT mill/ cu mm	HGB g/dl	HCT %	PLATELETS thsn/ cu mm	COUNT thsn/ cu mm	METHB %
3000	1	7.02	14.7	42.6	776	3.5	2.2
	2	7.96	15.0	43.0	918	3.9	2.3
	3	8.15	15.4	44.8	917	4.5	1.7
	4	7.88	14.5	44.3	837	4.1	2.7
	5	7.74	14.0	42.7	852	3.4	1.9
	6	7.80	14.5	42.5	801	3.6	2.3
	7	7.96	14.7	46.1	880	3.1	2.0
	8	7.33	14.0	40.7	874	3.6	2.7
	9	7.69	14.3	42.6	900	4.2	2.5
	10	7.49	14.2	42.9	779	2.9	2.0
1000	11	7.92	14.9	41.9	757	4.6	1.2
	12	8.01	15.0	44.0	725	3.1	0.6
	13	7.96	14.9	43.4	781	3.4	1.4
	14	8.15	15.3	43.4	838	2.9	0.6
	15	8.10	15.0	44.0	748	4.4	1.0
	16	8.45	15.8	46.3	805	3.1	1.1
	17	7.91	14.9	42.2	909	3.7	1.6
	18	8.10	15.1	43.4	880	4.1	1.0
	19	8.19	15.6	43.9	919	3.9	1.4
	20	8.39	15.3	46.0	752	3.7	1.0
200	21	8.03	15.3	43.4	757	3.1	0.1
	22	7.94	15.1	42.5	826	4.4	0.2
	23	8.50	15.6	46.9	815	3.6	1.0
	24	8.65	16.5	45.9	769	2.6	0.7
	25	7.83	14.9	41.8	761	3.2	0.7
	26	8.17	15.5	45.1	725	3.3	0.8
	27	8.34	15.6	44.2	762	2.9	0.6
	28	8.32	16.3	46.3	703	4.0	0.7
	29	8.48	16.5	46.4	830	4.0	0.8
	30	8.01	15.3	43.0	633	3.0	1.2
0	31	8.02	15.7	42.9	790	3.5	0.1
	32	8.66	15.7	46.9	669	3.2	1.0
	33	8.08	15.2	44.1	729	4.1	0.4
	34	8.26	15.5	45.3	748	4.3	0.4
	35	8.26	15.5	44.5	729	5.2	0.7
	36	8.03	15.1	42.6	731	5.1	0.3
	37	8.10	15.7	42.9	749	3.5	0.9
	38	8.17	16.0	44.5	753	3.8	1.0
	39	8.28	16.1	45.3	761	4.8	0.8
	40	8.51	16.1	47.1	766	3.9	0.3

Hematology Data/Females
90 Days

DOSE GROUPS	ANIMAL	MCV	MCH	MCHC	NEUTRO- PHILS	LYMPHO- CYTES	HEINZ BODIES	HEINZ RETIC
(mg tetryl/kg) diet	#	cumicr	picogm	g/dl	%	%	%	%
3000	1	54.6	18.8	34.5	23.3	73.2	0.0	2.3
	2	54.1	18.8	34.9	16.5	78.8	0.0	2.5
	3	55.0	18.9	34.4	15.9	80.2	0.0	3.0
	4	56.2	18.4	32.8	18.7	77.8	0.0	3.0
	5	55.2	18.1	32.8	18.2	77.6	0.0	1.8
	6	54.5	18.6	34.1	17.6	78.2	0.0	2.7
	7	57.9	18.5	32.0	23.9	68.1	0.0	2.7
	8	55.5	19.1	34.4	13.4	83.4	0.0	2.6
	9	55.4	18.6	33.5	15.5	81.3	0.0	2.8
	10	57.2	19.0	33.3	19.7	75.4	0.0	2.9
1000	11	52.8	18.8	35.7	19.8	76.7	0.0	2.0
	12	55.0	18.7	34.0	21.7	73.2	0.0	2.1
	13	54.5	18.7	34.4	20.4	75.7	0.0	2.0
	14	53.3	18.7	35.1	24.7	70.9	0.0	2.5
	15	54.3	18.5	34.0	26.6	68.6	0.0	2.4
	16	54.8	18.7	34.1	20.4	74.4	0.0	1.5
	17	53.3	18.9	35.4	22.5	73.6	0.0	2.0
	18	53.6	18.7	34.8	23.3	71.6	0.0	1.9
	19	53.6	19.1	35.5	21.4	75.1	0.0	2.0
	20	54.9	18.2	33.2	22.5	72.3	0.0	2.2
200	21	54.0	19.1	35.3	19.3	75.8	0.0	1.8
	22	53.5	19.0	35.5	15.8	80.9	0.0	1.7
	23	55.1	18.3	33.2	18.2	76.7	0.0	1.5
	24	53.1	19.1	36.0	18.6	77.3	0.0	2.1
	25	53.5	19.1	35.7	23.3	71.3	0.0	1.7
	26	55.2	19.0	34.4	29.2	66.9	0.0	1.6
	27	53.0	18.7	35.3	14.7	82.0	0.0	2.1
	28	55.6	19.6	35.3	20.3	75.2	0.0	1.5
	29	54.7	19.5	35.7	16.2	80.6	0.0	1.8
	30	53.7	19.1	35.6	27.1	68.2	0.0	1.9
0	31	53.5	19.5	36.5	20.4	75.3	0.0	1.7
	32	54.1	18.2	33.6	19.5	76.6	0.0	2.2
	33	54.6	18.9	34.6	20.8	74.1	0.0	1.8
	34	54.8	18.7	34.1	18.6	77.0	0.0	1.4
	35	53.9	18.7	34.7	26.8	68.0	0.0	1.5
	36	53.0	18.8	35.6	23.3	73.4	0.0	2.2
	37	52.9	19.4	36.6	14.9	82.0	0.0	1.6
	38	54.5	19.5	35.9	17.3	79.0	0.0	1.6
	39	54.7	19.4	35.5	19.6	74.9	0.0	1.6
	40	55.4	19.0	34.2	17.0	77.2	0.0	1.5

Hematology Data/Males
90 Days

DOSE GROUPS	ANIMAL #	RBC			WBC		
		COUNT	HGB	HCT	PLATELETS	COUNT	METHB
(mg tetryl/kg) diet		mill/ cu mm	g/dl	%	thsn/ cu mm	thsn/ cu mm	%
3000	41	8.98	14.3	44.7	891	4.6	2.8
	42	8.97	14.1	44.4	857	5.4	3.0
	43	9.03	14.3	46.3	801	4.5	2.2
	44	8.63	13.7	43.9	795	4.3	3.6
	45	8.96	14.4	44.7	889	4.1	3.3
	46	9.14	14.4	45.4	927	3.6	2.1
	47	9.15	14.3	46.3	867	4.0	2.7
	48	8.61	13.9	44.1	839	5.4	1.9
	49	8.92	14.5	44.0	897	4.3	2.4
	50	9.02	14.3	46.0	804	4.1	2.7
1000	51	9.18	15.1	46.8	806	5.2	0.9
	52	9.23	15.5	47.2	780	4.1	1.5
	53	9.04	15.0	45.4	824	4.6	1.7
	54	9.33	15.4	47.0	753	3.5	1.4
	55	9.11	15.1	46.6	723	4.8	1.2
	56	9.50	15.6	48.8	584	3.6	1.4
	57	9.59	15.6	49.1	649	4.8	1.2
	58	9.19	15.1	45.4	846	3.8	1.1
	59	9.44	15.5	47.9	797	3.7	1.7
	60	9.12	15.2	47.3	689	4.9	1.6
200	61	9.60	16.0	48.4	770	4.5	0.9
	62	9.64	15.9	49.5	808	3.7	0.0
	63	9.21	16.0	47.7	675	4.3	0.9
	64	9.29	15.5	47.9	727	4.4	0.9
	65	9.43	16.3	48.9	677	3.5	0.9
	66	9.50	15.2	49.6	720	5.9	0.3
	67	8.98	15.1	46.4	749	3.9	0.6
	68	9.10	15.2	46.2	682	3.8	0.6
	69	9.31	15.5	48.1	750	3.8	0.4
	70	9.04	15.4	47.8	725	4.3	0.3
0	71	9.37	16.1	48.4	705	3.6	0.6
	72	9.27	15.6	47.9	688	4.6	0.3
	73	9.55	15.9	48.3	803	4.9	0.2
	74	9.25	15.9	48.5	738	5.1	0.3
	75	9.44	15.9	49.6	718	4.3	1.1
	76	9.62	15.9	49.7	685	4.4	0.5
	77	9.24	15.9	48.4	607	3.1	0.1
	78	8.97	15.3	47.2	935	3.9	0.2
	79	9.44	16.0	47.5	762	4.9	1.3
	80	9.23	15.8	48.2	696	4.7	0.4

Hematology Data/Males
90 Days

DOSE GROUPS	ANIMAL	MCV	MCH	MCHC	NEUTRO- PHILS	LYMPHO- CYTES	HEINZ BODIES	RETIC
(mg tetryl/kg)	diet	#	cumicr	picogm	g/dl	%	%	%
3000	41	49.7	15.9	32.1	27.4	68.9	0.0	3.4
	42	49.5	15.8	31.9	24.8	71.4	0.0	3.4
	43	51.3	15.8	30.9	25.5	69.1	0.0	3.4
	44	50.9	15.9	31.3	24.2	72.6	0.0	3.4
	45	49.8	16.1	32.2	24.7	71.6	0.0	3.5
	46	49.7	15.8	31.7	26.7	67.9	0.0	3.4
	47	50.6	15.7	31.0	23.2	76.2	0.0	3.3
	48	51.2	16.1	31.4	21.4	74.9	0.0	3.1
	49	49.3	16.2	32.8	24.6	71.4	0.0	3.6
	50	51.0	15.9	31.1	27.1	67.6	0.0	3.0
1000	51	50.9	16.4	32.2	19.9	75.7	0.0	2.0
	52	51.1	16.8	32.8	21.2	75.1	0.0	2.0
	53	50.2	16.6	33.0	28.9	66.6	0.0	2.1
	54	50.4	16.5	32.7	29.7	65.0	0.0	2.0
	55	51.1	16.6	32.4	26.7	67.3	0.0	2.0
	56	51.4	16.4	31.9	32.7	62.7	0.0	2.1
	57	51.3	16.3	31.8	24.4	70.2	0.0	1.8
	58	49.4	16.4	33.2	25.1	68.8	0.0	2.1
	59	50.8	16.4	32.3	21.2	75.4	0.0	2.3
	60	51.9	16.7	32.2	28.6	66.1	0.0	2.1
200	61	50.4	16.7	33.2	23.7	71.9	0.0	1.8
	62	51.4	16.4	32.0	27.7	67.9	0.0	1.6
	63	51.8	17.4	33.6	22.0	74.5	0.0	1.8
	64	51.5	16.7	32.5	22.1	74.0	0.0	1.6
	65	51.8	17.3	33.3	28.5	66.1	0.0	2.0
	66	52.2	16.0	30.6	18.7	76.3	0.0	1.7
	67	51.7	16.8	32.6	22.5	73.4	0.0	2.1
	68	50.8	16.7	32.9	20.9	74.6	0.0	2.1
	69	51.6	16.6	32.2	22.5	71.4	0.0	2.1
	70	52.9	17.0	32.2	16.9	78.6	0.0	2.0
0	71	51.6	17.2	33.3	24.5	70.3	0.0	2.1
	72	51.7	16.8	32.6	22.6	72.9	0.0	2.0
	73	50.6	16.7	33.0	18.6	77.3	0.0	2.0
	74	52.5	17.2	32.7	22.1	74.7	0.0	1.9
	75	52.6	16.8	32.1	18.9	75.6	0.0	2.2
	76	51.7	16.5	31.9	20.1	76.6	0.0	1.8
	77	52.3	17.2	32.9	27.7	68.7	0.0	2.0
	78	52.6	17.0	32.4	29.3	64.1	0.0	2.2
	79	50.3	16.9	33.6	21.2	75.7	0.0	1.6
	80	52.2	17.1	32.8	18.8	77.2	0.0	1.8

APPENDIX E

CLINICAL CHEMISTRY

DATA

Clinical Chemistries/Females
45 Days

DOSE (mg tetryl/kg) diet	GROUPS	ANIMAL #	GLUCOSE CREATININE		BUN mg/dl	Na mmol/l	TOTAL PROTEIN g/dl	TOTAL BILIRUBIN mg/dl	AST U/L
			mg/dl	mg/dl					
3000	401	94	0.6	18	140	6.2	0.3	198	
	402	136	0.6	14	139	6.8	0.3	150	
	403	142	0.6	19	139	6.3	0.2	104	
	404	139	0.6	18	140	5.7	0.2	135	
	405	140	0.6	17	140	6.4	0.3	149	
1000	406	171	0.7	18	140	6.5	0.2	203	
	407	130	0.7	18	142	6.6	0.2	328	
	408	169	0.6	17	140	6.5	0.2	108	
	409	164	0.6	16	139	6.4	0.2	175	
	410	173	0.6	16	137	6.6	0.2	97	
200	411	169	0.5	15	138	6.1	0.2	90	
	412	162	0.6	19	139	6.2	0.1	99	
	413	173	0.5	19	139	6.0	0.1	86	
	414	165	0.6	17	139	6.1	0.1	88	
	415	161	0.5	18	138	5.8	0.2	113	
0	416	131	0.5	17	139	6.1	0.2	111	
	417	164	0.5	18	137	6.0	0.1	103	
	418	167	0.5	21	138	6.3	0.2	95	
	419	178	0.5	14	137	5.9	0.2	75	
	420	134	0.6	22	141	6.7	0.2	147	

Clinical Chemistries/Females
45 Days

DOSE GROUPS (mg tetryl/kg) diet	ANIMAL #	ALT U/L	AP U/L	K mmol/l	Ca mg/dl	ALBUMIN			TRIG mg/dl	PHOS mg/dl
							g/dl	mg/dl		
3000	401	45	94	4.9	10.9	4.5		27	10.4	
	402	30	125	4.3	10.9	5.0		35	8.8	
	403	33	104	4.0	10.6	4.6		31	8.8	
	404	42	136	4.4	10.4	4.1		27	7.4	
	405	41	121	5.1	10.7	4.7		27	11.8	
1000	406	98	131	4.4	11.1	4.7		60	10.5	
	407	99	81	4.3	11.1	4.8		65	12.0	
	408	34	120	4.1	10.9	4.5		43	8.9	
	409	40	141	4.2	10.8	4.6		40	10.3	
	410	30	139	4.5	10.9	4.8		30	8.4	
200	411	26	128	4.5	10.7	4.3		32	7.8	
	412	39	89	4.2	10.5	4.3		32	8.1	
	413	38	103	4.9	10.9	4.4		55	9.1	
	414	40	153	3.9	10.5	4.1		45	8.7	
	415	35	140	5.1	10.4	4.0		30	8.2	
0	416	38	105	4.1	10.5	4.4		54	7.5	
	417	37	123	4.3	10.5	4.3		41	8.8	
	418	38	129	4.7	10.7	4.4		31	9.1	
	419	31	126	5.0	10.6	4.3		35	8.2	
	420	43	133	4.8	11.0	4.5		37	10.9	

Clinical Chemistries/Males
45 Days

DOSE GROUPS (mg tetryl/kg) diet	ANIMAL #	GLUCOSE CREATININE		BUN	Na	TOTAL PROTEIN	TOTAL BILIRUBIN	AST
		mg/dl	mg/dl	mg/dl	mmol/l	g/dl	mg/dl	U/L
3000	421	169	0.6	18	139	7.4	0.2	98
	422	186	0.6	16	138	7.2	0.1	116
	423	171	0.6	19	138	7.0	0.2	95
	424	165	0.6	19	139	7.0	0.2	105
	425	185	0.6	18	138	7.0	0.2	144
1000	426	200	0.6	19	139	6.7	0.1	106
	427	168	0.6	20	141	7.0	0.1	197
	428	212	0.7	23	138	6.9	0.2	101
	429	175	0.6	20	139	7.0	0.1	121
	430	171	0.6	20	138	6.8	0.1	147
200	431	176	0.5	19	140	6.7	0.1	107
	432	168	0.6	15	139	6.4	0.1	98
	433	209	0.6	19	138	6.6	0.1	120
	434	177	0.5	16	138	6.4	0.3	113
	435	188	0.6	23	140	6.9	0.1	130
0	436	187	0.6	20	139	6.4	0.1	130
	437	229	0.6	22	136	6.2	0.1	123
	438	170	0.6	18	138	6.5	0.1	112
	439	188	0.5	19	136	6.2	0.3	153
	440	199	0.7	19	139	6.2	0.1	116

Clinical Chemistries/Males
45 Days

DOSE GROUPS		ANIMAL	ALT	AP	K	Ca	ALBUMIN	TRIG	PHOS
(mg tetryl/kg) diet	#		U/L	U/L	mmol/l	mg/dl	g/dl	mg/dl	mg/dl
3000	421		41	131	6.3	11.3	5.1	106	11.6
	422		40	102	5.5	11.0	5.1	62	10.0
	423		30	125	6.0	11.3	4.9	58	12.2
	424		31	111	4.9	11.1	5.1	55	10.2
	425		51	129	5.4	11.0	5.0	40	10.1
1000	426		34	126	5.6	11.1	4.5	49	10.2
	427		92	110	4.7	10.8	4.9	105	9.4
	428		39	127	4.7	11.2	4.9	102	9.9
	429		46	137	4.6	11.1	4.8	124	10.3
	430		47	119	4.5	10.9	4.8	105	9.4
200	431		50	155	4.4	10.9	4.7	72	9.4
	432		36	131	5.0	10.8	4.3	53	10.5
	433		54	122	4.3	10.8	4.7	137	8.9
	434		44	120	5.6	10.7	4.5	45	9.5
	435		45	142	4.2	10.8	5.0	136	9.9
0	436		66	134	4.5	10.6	4.4	76	9.2
	437		50	134	4.4	10.4	4.3	137	9.7
	438		37	151	4.4	10.7	4.5	107	9.6
	439		67	131	5.6	10.7	4.4	91	10.0
	440		49	129	4.8	10.8	4.3	88	10.6

Clinical Chemistries/Females
90 Days

DOSE GROUPS (mg tetryl/kg) diet	#	ANIMAL	GLUCOSE	CREATININE	BUN	Na	TOTAL PROTEIN	TOTAL BILIRUBIN	AST
			mg/dl	mg/dl	mg/dl	mmol/l	g/dl	mg/dl	U/L
3000	1	117	0.6	18	145	6.9	0.2	183	
	2	109	0.5	17	145	6.8	0.2	146	
	3	132	0.6	19	142	6.8	0.2	223	
	4	134	0.6	25	143	6.9	0.2	126	
	5	137	0.5	20	144	6.4	0.2	102	
	6	126	0.5	19	142	6.5	0.3	169	
	7	172	0.6	24	143	7.2	0.3	172	
	8	120	0.6	19	144	6.9	0.2	143	
	9	134	0.6	22	143	6.7	0.2	170	
	10	119	0.6	22	144	6.0	0.2	159	
1000	11	163	0.5	18	142	6.5	0.2	178	
	12	119	0.6	24	142	6.8	0.3	197	
	13	149	0.6	22	142	6.6	0.1	132	
	14	145	0.5	18	144	6.5	0.1	144	
	15	164	0.6	18	142	6.5	0.1	147	
	16	144	0.6	24	143	6.2	0.1	245	
	17	116	0.5	19	144	6.7	0.2	133	
	18	153	0.5	21	142	6.5	0.1	118	
	19	130	0.6	19	142	6.7	0.2	148	
	20	170	0.6	19	145	6.2	0.2	165	
200	21	145	0.5	19	142	6.3	0.2	133	
	22	128	0.6	18	143	6.1	0.1	170	
	23	145	0.6	19	143	6.2	0.1	266	
	24	155	0.5	17	143	6.2	0.2	117	
	25	165	0.6	21	143	6.4	0.2	133	
	26	114	0.6	20	143	6.9	0.4	316	
	27	143	0.5	18	144	6.4	0.1	155	
	28	132	0.6	23	142	6.7	0.3	174	
	29	121	0.5	17	144	6.5	0.2	126	
	30	140	0.5	18	142	6.0	0.1	212	
0	31	97	0.5	17	143	6.3	0.2	130	
	32	124	0.6	16	144	6.3	0.1	199	
	33	128	0.5	21	143	6.4	0.1	127	
	34	139	0.6	20	142	6.2	0.1	140	
	35	117	0.6	19	142	6.3	0.1	141	
	36	159	0.5	16	142	5.9	0.1	102	
	37	130	0.5	17	142	5.8	0.1	95	
	38	107	0.5	16	142	6.2	0.1	123	
	39	136	0.5	19	143	6.1	0.1	134	
	40	114	0.6	22	144	6.3	0.1	129	

Clinical Chemistries/Females
90 Days

DOSE GROUPS (mg tetryl/kg) diet	ANIMAL #	ALT U/L	AP U/L	K mmol/l	Ca mg/dl	ALBUMIN g/dl	TRIG mg/dl	PHOS mg/dl	CHOL mg/dl
3000	1	71	62	4.1	10.2	5.0	25	9.1	134
	2	40	59	3.9	10.0	4.9	27	9.1	145
	3	84	51	4.6	10.3	4.8	20	8.9	128
	4	43	69	4.1	10.5	5.1	28	8.3	132
	5	40	68	4.6	10.2	4.8	24	7.8	142
	6	64	63	3.7	9.9	4.6	25	8.0	115
	7	75	70	6.8	11.4	5.4	31	11.2	144
	8	43	47	4.6	10.4	5.0	21	9.6	128
	9	71	65	4.5	10.5	5.0	31	9.6	129
	10	59	79	4.7	10.0	5.0	22	9.6	118
1000	11	108	60	3.8	9.9	4.6	30	8.4	112
	12	76	87	4.5	10.1	4.9	41	10.1	132
	13	61	66	4.3	10.3	4.8	27	7.9	129
	14	55	62	4.6	9.9	4.6	21	8.4	110
	15	76	69	4.4	10.0	4.7	31	7.7	126
	16	150	66	5.0	10.4	4.5	21	9.8	120
	17	49	63	4.0	10.1	4.8	30	7.8	127
	18	66	66	4.1	10.4	4.8	52	7.3	125
	19	66	64	5.0	10.5	4.8	54	9.7	136
	20	91	76	5.1	10.2	4.7	55	8.6	113
200	21	48	80	4.3	10.2	4.6	64	9.0	115
	22	46	70	4.0	10.0	4.5	51	7.8	101
	23	193	71	5.0	10.5	4.4	21	11.0	113
	24	60	65	4.8	10.0	4.6	35	7.6	119
	25	67	79	4.8	10.3	4.5	58	8.7	95
	26	92	54	5.2	10.4	5.1	58	9.0	117
	27	87	67	4.4	9.9	4.6	25	8.8	113
	28	82	86	4.1	10.6	5.0	57	8.5	119
	29	47	60	4.7	10.1	4.8	42	9.0	125
	30	132	108	3.6	10.3	4.6	35	6.9	112
0	31	38	59	4.2	10.1	4.3	32	9.0	113
	32	105	74	4.1	9.8	4.4	29	7.7	104
	33	57	85	3.9	10.4	4.6	71	7.8	105
	34	49	90	4.3	10.1	4.5	32	9.3	95
	35	57	94	4.1	10.2	4.3	39	9.4	100
	36	49	77	3.7	9.6	4.3	27	6.4	96
	37	39	65	4.0	9.9	4.2	38	8.0	93
	38	42	64	4.4	10.0	4.4	33	8.7	108
	39	61	78	3.6	10.3	4.6	51	7.6	102
	40	55	79	4.0	10.0	4.6	54	9.2	111

Clinical Chemistries/Males
90 Days

DOSE GROUPS (mg tetryl/kg) diet	#	ANIMAL	GLUCOSE	CREATININE	BUN	Na	TOTAL PROTEIN	TOTAL BILIRUBIN	AST
			mg/dl	mg/dl	mg/dl	mmol/l	g/dl	mg/dl	U/L
3000	41		178	0.6	20	142	7.3	0.1	158
	42		165	0.6	19	143	7.3	0.1	168
	43		207	0.6	22	143	7.8	0.1	137
	44		176	0.6	20	142	6.8	0.1	168
	45		161	0.5	22	142	7.6	0.1	188
	46		178	0.7	22	143	7.7	0.1	168
	47		185	0.6	21	142	7.5	0.1	233
	48		198	0.6	22	142	7.1	0.1	144
	49		152	0.6	20	143	7.3	0.1	221
	50		201	0.6	22	141	7.5	0.1	170
1000	51		211	0.6	24	142	7.2	0.1	138
	52		187	0.6	22	142	7.0	0.0	167
	53		167	0.7	22	143	7.1	0.1	152
	54		181	0.6	23	144	7.0	0.1	161
	55		194	0.6	21	143	7.4	0.1	155
	56		192	0.6	21	143	7.2	0.1	220
	57		208	0.6	23	142	7.7	0.1	173
	58		161	0.6	23	144	7.0	0.1	152
	59		185	0.6	21	144	7.2	0.1	168
	60		189	0.6	22	143	7.4	0.1	160
200	61		198	0.6	22	145	6.8	0.1	148
	62		206	0.6	21	144	7.1	0.1	106
	63		195	0.6	20	144	6.8	0.1	182
	64		206	0.6	20	143	7.1	0.1	158
	65		190	0.6	19	145	6.8	0.1	183
	66		210	0.6	24	143	6.9	0.1	132
	67		153	0.7	19	142	6.9	0.1	134
	68		182	0.7	20	143	6.7	0.1	189
	69		171	0.6	17	144	6.8	0.1	110
	70		164	0.6	24	142	6.9	0.1	161
0	71		168	0.6	20	143	6.8	0.1	129
	72		183	0.6	20	142	7.2	0.0	159
	73		222	0.6	21	144	6.9	0.1	121
	74		210	0.7	21	142	6.9	0.0	130
	75		185	0.7	20	143	6.9	0.1	198
	76		191	0.6	21	145	6.9	0.1	239
	77		175	0.6	18	143	6.6	0.0	213
	78		170	0.6	20	143	6.4	0.1	121
	79		168	0.6	20	143	6.7	0.0	131
	80		184	0.6	21	142	6.8	0.0	129

Clinical Chemistries/Males
90 Days

DOSE		ANIMAL	ALT	AP	K	Ca	ALBUMIN	TRIG	PHOS	CHOL
GROUPS	(mg tetryl/kg) diet	#	U/L	U/L	mmol/l	mg/dl	g/dl	mg/dl	mg/dl	mg/dl
3000	41	52	75	5.0	10.5	5.1	40	9.5	100	
	42	62	68	4.4	10.6	5.1	67	7.5	99	
	43	58	87	5.1	10.7	5.3	98	8.8	112	
	44	73	80	4.9	10.6	5.0	64	9.0	94	
	45	58	84	5.1	10.9	5.3	130	9.7	109	
	46	62	86	5.3	11.1	5.2	109	10.6	97	
	47	86	78	5.0	10.7	5.3	80	8.4	110	
	48	60	80	5.0	10.4	4.6	136	8.0	118	
	49	75	81	5.2	10.6	5.2	110	9.4	107	
	50	79	90	5.0	10.9	5.1	59	8.8	108	
1000	51	71	97	4.5	10.7	5.0	130	7.9	78	
	52	88	92	4.3	10.3	4.8	113	8.9	75	
	53	73	79	4.5	10.6	5.0	108	8.5	75	
	54	65	82	4.5	10.9	5.0	106	8.1	73	
	55	85	76	4.5	10.7	5.0	98	8.5	80	
	56	119	95	4.5	10.5	5.0	123	7.3	84	
	57	89	103	4.8	10.9	5.2	180	8.1	87	
	58	69	81	4.3	10.7	4.9	122	9.8	81	
	59	80	89	5.6	10.8	5.0	71	10.6	75	
	60	65	89	4.7	10.6	5.1	143	8.2	83	
200	61	86	92	4.4	10.4	4.8	148	8.5	65	
	62	67	101	5.4	11.0	4.9	92	8.4	66	
	63	93	86	4.5	10.7	4.9	137	8.4	72	
	64	92	100	4.5	10.5	5.0	112	8.6	66	
	65	90	86	5.3	10.7	4.9	98	10.3	63	
	66	72	93	5.2	10.5	4.9	146	9.3	73	
	67	68	95	4.6	10.6	4.6	73	8.8	59	
	68	124	87	4.8	10.4	4.7	70	9.7	63	
	69	65	92	4.9	10.6	4.8	77	8.3	73	
	70	81	105	4.4	10.6	4.7	81	9.2	64	
0	71	77	102	4.5	10.6	4.8	114	9.4	57	
	72	80	113	5.0	10.7	4.9	141	9.0	62	
	73	59	107	4.3	10.5	4.9	150	8.9	75	
	74	78	112	4.4	10.4	4.7	85	8.8	49	
	75	89	97	4.6	10.4	4.7	109	9.8	61	
	76	158	110	5.0	10.3	4.8	121	9.9	59	
	77	105	106	5.0	10.5	4.8	89	9.0	59	
	78	67	103	5.0	10.5	4.4	84	8.0	51	
	79	73	91	4.3	10.4	4.7	62	9.0	57	
	80	65	108	4.4	10.4	4.5	89	8.7	56	

APPENDIX F

CLINICAL OBSERVATIONS

CLINICAL OBSERVATIONS

DATE	DAILY OBSERVATIONS
01/12/94	Initial food, water, and animals weighed for the females. Feeders changed. All animals look normal.
01/13/94	Initial food, water, and animals weighed for the males. Feeders changed. All animals look normal.
01/18/94	Food, water, and animals weighed for both females and males. Feeders changed. All animals look normal.
01/19/94	All animals look normal.
01/20/94	All animals look normal.
01/21/94	Food and water weighed for the both females and males. All animals look normal.
01/24/94	All animals look normal.
01/25/94	Food, water, and animals weighed for the both females and males. All animals look normal.
01/26/94	All animals look normal.
01/27/94	All animals look normal.
01/28/94	Food and water weighed for the both females and males. All animals look normal.
01/31/94	All animals look normal.
02/01/94	Food, water, and animals weighed for the both females and males. All animals look normal.
02/02/94	All animals look normal.
02/03/94	All animals look normal.
02/04/94	Food and water weighed for the both females and males. All animals look normal.
02/07/94	All animals look normal.
02/08/94	Food, water, and animals weighed for the both females and males. All animals look normal.
02/09/94	All animals look normal.
02/10/94	All animals look normal.
02/11/94	Food and water weighed for the both females and males. All animals look normal.

CLINICAL OBSERVATIONS

DAILY
OBSERVATIONS

DATE	OBSERVATIONS
02/14/94	All animals look normal.
02/15/94	Food, water, and animals weighed for the both females and males. All animals look normal.
02/16/94	All animals look normal.
02/17/94	All animals look normal.
02/18/94	Food and water weighed for the both females and males. All animals look normal.
02/22/94	Food, water, and animals weighed for the both females and males. All animals look normal.
02/23/94	All animals look normal.
02/24/94	All animals look normal.
02/25/94	Food and water weighed for the both females and males. All animals look normal.
02/28/94	All animals look normal.
03/01/94	Food, water, and animals weighed for the both females and males. Feeders changed. All animals look normal.
03/02/94	All animals look normal.
03/03/94	All animals look normal.
03/04/94	Food and water weighed for the both females and males. All animals look normal.
03/07/94	All animals look normal.
03/08/94	Food, water, and animals weighed for the both females and males. Feeders changed. All animals look normal.
03/10/94	All animals look normal.
03/11/94	Food and water weighed for the both females and males. All animals look normal.
03/14/94	All animals look normal.
03/15/94	Food, water, and animals weighed for the both females and males. Feeders changed. All animals look normal.
03/17/94	All animals look normal.
03/18/94	Food and water weighed for the both females and males. All animals look normal.

CLINICAL OBSERVATIONS

DATE	DAILY OBSERVATIONS
03/21/94	All animals look normal.
03/22/94	Food, water, and animals weighed for the both females and males. Feeders changed. All animals look normal.
03/23/94	All animals look normal.
03/24/94	All animals look normal.
03/25/94	Food and water weighed for the both females and males. All animals look normal.
03/28/94	All animals look normal.
03/29/94	Food, water, and animals weighed for the both females and males. Feeders changed. All animals look normal.
03/30/94	All animals look normal.
03/31/94	All animals look normal.
04/01/94	Food and water weighed for the both females and males. All animals look normal.
04/04/94	All animals look normal.
04/05/94	Food, water, and animals weighed for the both females and males. Feeders changed. All animals look normal.
04/06/94	All animals look normal.
04/07/94	All animals look normal.
04/08/94	Food and water weighed for the both females and males. All animals look normal.
04/11/94	All animals look normal.
04/12/94	Final food and water weights taken. Animals weighed. #1-#40 females taken off food for sacrifice 4-13-94.
04/13/94	All animals look normal. Final food and water weights taken. Animals weighed. #41-#80 males taken off food for sacrifice 4-14-94. Animals 1-40 were sacrificed. All other animals look normal.
04/14/94	Animals 41-80 were sacrificed.

APPENDIX G

**GROSS AND
HISTOPATHOLOGY
DATA**

REPORTS CODE TABLE

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unavailable/unsuitable for evaluation
*	Tissues not examined/not required by protocol
()	Focal
<>	Multifocal
□	Diffuse
1	Minimal
2	Mild
3	Moderate
4	Marked

Abbreviation List

NOS

Not Otherwise Specified

(End of Report)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	NUMBER OF ANIMALS:	1		2		3		4	
		10	10	10	10	10	10	10	10
BRAIN	# EX	10		0		0		10	
NERVE	# EX	10		0		0		10	
SPINAL CORD	# EX	10		0		0		10	
SALIVARY GLAND	# EX	10		0		0		10	
PANCREAS	# EX	10		0		0		10	
MANDIBULAR LYMPH NODE	# EX	10		0		0		10	
ZYMBAL'S GLAND	# EX	10		0		0		10	
PITUITARY	# EX	10		0		0		10	
ADRENALS	# EX	10		0		0		10	
THYROID	# EX	10		0		0		10	
PARATHYROID	# EX	9		0		0		8	
TRACHEA	# EX	10		0		0		10	
ESOPHAGUS	# EX	10		0		0		10	
THYMUS	# EX	10		0		0		10	
Hemorrhage		1	10.0	0	0.0	0	0.0	3	30.0
HEART	# EX	10		0		0		10	
Inflammation, Chronic		1	10.0	0	0.0	0	0.0	1	10.0
COLON	# EX	10		0		0		10	

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP: NUMBER OF ANIMALS:	1		2		3		4	
	10		10		10		10	
JEJUNUM	# EX	10		0		0		10
AORTA	# EX	10		0		0		10
LIVER	# EX	10		0		0		10
Inflammation, Subacute		1	10.0	0	0.0	0	0.0	0 0.0
Inflammation, Chronic		0	0.0	0	0.0	0	0.0	1 10.0
SPLEEN	# EX	10		10		10		10
Hyperplasia, Erythroid Cell		1	10.0	0	0.0	0	0.0	0 0.0
Pigmentation, NOS		7	70.0	3	30.0	0	0.0	4 40.0
Fibrosis		1	10.0	1	10.0	2	20.0	0 0.0
Depletion, Lymphoid		0	0.0	1	10.0	0	0.0	0 0.0
TONGUE	# EX	10		1		0		10
SKELETAL MUSCLE	# EX	10		1		0		10
LUNGS	# EX	10		1		0		10
Inflammation, Chronic		2	20.0	0	0.0	0	0.0	1 10.0
KIDNEYS	# EX	10		10		10		10
Mineralization, NOS		9	90.0	9	90.0	10	100.0	9 90.0
Pigmentation, Tubular Epithelium		10	100.0	10	100.0	0	0.0	0 0.0
Regeneration, Tubular		0	0.0	1	10.0	0	0.0	0 0.0
Lymphocytic Infiltrates		0	0.0	0	0.0	0	0.0	1 10.0
URINARY BLADDER	# EX	10		0		0		10
STOMACH	# EX	10		0		0		10
DUODENUM	# EX	10		0		0		10
ILEUM	# EX	10		0		0		10

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP: NUMBER OF ANIMALS:	1		2		3		4	
	10		10		10		10	
CECUM	# EX	10		0		0		10
RECTUM	# EX	10		0		0		10
MESENTERIC LYMPH NODE	# EX	10		0		0		10
OVARIES	# EX	10		0		0		10
Cyst, NOS		0	0.0	0	0.0	0	0.0	1 10.0
UTERUS	# EX	10		0		0		10
Dilatation, Bilateral		3	30.0	0	0.0	0	0.0	4 40.0
SKIN	# EX	10		0		0		10
CLITORAL GLANDS	# EX	10		0		0		10
Lymphocytic Infiltrates		1	10.0	0	0.0	0	0.0	5 50.0
Inflammation, Suppurative		0	0.0	0	0.0	0	0.0	1 10.0
EYES	# EX	10		0		0		10
Microgranuloma, Cornea		1	10.0	0	0.0	0	0.0	5 50.0
HARDERIAN GLAND	# EX	10		0		0		10
Lymphocytic Infiltrates		3	30.0	0	0.0	0	0.0	1 10.0
FEMUR/STERNUM	# EX	10		0		0		10
NASAL	# EX	10		0		0		10
Inflammation, Subacute		0	0.0	0	0.0	0	0.0	1 10.0
MAMMARY GLAND	# EX	10		0		0		10

Incidence Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	NUMBER OF ANIMALS:	5		6		7		8	
		10		10		10		10	
BRAIN	# EX	10		0		0		10	
NERVE	# EX	10		0		0		10	
SPINAL CORD	# EX	10		0		0		10	
SALIVARY GLAND	# EX	10		0		0		10	
PANCREAS	# EX	10		0		0		10	
Degeneration, Acinar		3	30.0	0	0.0	0	0.0	0	0.0
MANDIBULAR LYMPH NODE	# EX	10		0		0		10	
ZYMBAL'S GLAND	# EX	9		0		0		10	
PITUITARY	# EX	10		0		0		10	
Cyst, NOS, Pars Distalis		0	0.0	0	0.0	0	0.0	1	10.0
ADRENALS	# EX	10		0		0		10	
THYROID	# EX	10		0		0		10	
PARATHYROID	# EX	8		0		0		7	
TRACHEA	# EX	10		0		0		10	
ESOPHAGUS	# EX	10		0		0		10	
THYMUS	# EX	10		2		1		10	
Hemorrhage		3	30.0	2	100.0	1	100.0	4	40.0
HEART	# EX	10		0		0		10	
Degeneration, Myocardial		0	0.0	0	0.0	0	0.0	1	10.0
Inflammation, Chronic		1	10.0	0	0.0	0	0.0	2	20.0
Inflammation, Chronic/Active, Arterial		0	0.0	0	0.0	0	0.0	1	10.0

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:	NUMBER OF ANIMALS:	5		6		7		8	
		10		10		10		10	
COLON	# EX 10			0		0		10	
JEJUNUM	# EX 10			0		0		10	
AORTA	# EX 10			0		0		10	
LIVER	# EX 10			0		0		10	
SPLEEN	# EX 10			10		10		10	
Hyperplasia, Erythroid Cell	10 100.0			2 20.0		1 10.0		0 0.0	
Pigmentation, NOS	4 40.0			0 0.0		0 0.0		0 0.0	
Fibrosis	1 10.0			0 0.0		1 10.0		0 0.0	
TONGUE	# EX 10			0		0		10	
SKELETAL MUSCLE	# EX 10			0		0		10	
LUNGS	# EX 10			0		0		10	
Inflammation, Chronic	2 20.0			0 0.0		0 0.0		0 0.0	
KIDNEYS	# EX 10			10		10		10	
Mineralization, NOS	10 100.0			10 100.0		10 100.0		10 100.0	
Pigmentation, Tubular Epithelium	10 100.0			1 10.0		0 0.0		0 0.0	
Regeneration, Tubular	10 100.0			10 100.0		10 100.0		6 60.0	
Cytoplasmic Droplets	10 100.0			10 100.0		0 0.0		0 0.0	
Degeneration, Tubular	10 100.0			10 100.0		10 100.0		10 100.0	
Hyaline Casts	9 90.0			0 0.0		0 0.0		0 0.0	
URINARY BLADDER	# EX 10			0		0		10	
Urolith, NOS	3 30.0			0 0.0		0 0.0		1 10.0	
Hemorrhage	3 30.0			0 0.0		0 0.0		0 0.0	
PROSTATE	# EX 10			0		0		10	

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP: NUMBER OF ANIMALS:	5		6		7		8	
	10		10		10		10	
STOMACH	# EX	10		0		0		10
DUODENUM	# EX	10		0		0		10
ILEUM	# EX	10		0		0		10
CECUM	# EX	10		0		0		10
RECTUM	# EX	10		0		0		10
MESENTERIC LYMPH NODE	# EX	10		0		0		10
TESTES	# EX	10		0		0		10
EPIDIDYMIDES	# EX	10		0		0		10
SEMINAL VESICLE	# EX	10		0		0		10
SKIN	# EX	10		0		0		10
PREPUTIAL GLANDS	# EX	10		0		0		10
Inflammation, Chronic/Active		1	10.0	0	0.0	0	0.0	3 30.0
Inflammation, Suppurative		2	20.0	0	0.0	0	0.0	0 0.0
Lymphocytic Infiltrates		4	40.0	0	0.0	0	0.0	3 30.0
EYES	# EX	10		0		0		10
Microgranuloma, Cornea		3	30.0	0	0.0	0	0.0	4 40.0
HARDERIAN GLAND	# EX	10		0		0		10
FEMUR/STERNUM	# EX	10		0		0		10
Hyperplasia, Erythroid Cell		3	30.0	0	0.0	0	0.0	0 0.0
NASAL	# EX	10		0		0		10

Incidence Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

PROJECT SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:

5 6 7 8

NUMBER OF ANIMALS:

10 10 10 10

MAMMARY GLAND

	#	%	#	%	#	%	#	%
	# EX	10	0	0	0	10		

Incidence Calculated by No. of Tissues Scored

(END OF REPORT)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:	1	2	3	4
NUMBER OF ANIMALS:	10	10	10	10

	# EX	1	2	3	4
		# SEV	# SEV	# SEV	# SEV
BRAIN		10	0	0	10
NERVE		10	0	0	10
SPINAL CORD		10	0	0	10
SALIVARY GLAND		10	0	0	10
PANCREAS		10	0	0	10
MANDIBULAR LYMPH NODE		10	0	0	10
ZYMBAL'S GLAND		10	0	0	10
PITUITARY		10	0	0	10
ADRENALS		10	0	0	10
THYROID		10	0	0	10
PARATHYROID		9	0	0	8
TRACHEA		10	0	0	10
ESOPHAGUS		10	0	0	10
THYMUS		10	0	0	10
Hemorrhage		0.10	0.00	0.00	0.30
HEART		10	0	0	10
Inflammation, Chronic		0.10	0.00	0.00	0.10
COLON		10	0	0	10
JEJUNUM		10	0	0	10

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP:		1	2	3	4
NUMBER OF ANIMALS:		10	10	10	10
	# EX	# SEV	# SEV	# SEV	# SEV
AORTA	# EX 10	0	0	0	10
LIVER	# EX 10	0	0	0	10
Inflammation, Subacute	1 0.10	0 0.00	0 0.00	0 0.00	0 0.00
Inflammation, Chronic	0 0.00	0 0.00	0 0.00	1 0.10	
SPLEEN	# EX 10	10	10	10	10
Hyperplasia, Erythroid Cell	1 0.10	0 0.00	0 0.00	0 0.00	0 0.00
Pigmentation, NOS	7 1.00	3 0.30	0 0.00	4 0.40	
Fibrosis	1 0.10	1 0.20	2 0.30	0 0.00	
Depletion, Lymphoid	0 0.00	1 0.20	0 0.00	0 0.00	
TONGUE	# EX 10	1	0	0	10
SKELETAL MUSCLE	# EX 10	1	0	0	10
LUNGS	# EX 10	1	0	0	10
Inflammation, Chronic	2 0.20	0 0.00	0 0.00	1 0.10	
KIDNEYS	# EX 10	10	10	10	10
Mineralization, NOS	9 1.00	9 0.90	10 1.20	9 1.20	
Pigmentation, Tubular Epithelium	10 2.40	10 1.10	0 0.00	0 0.00	
Regeneration, Tubular	0 0.00	1 0.10	0 0.00	0 0.00	
Lymphocytic Infiltrates	0 0.00	0 0.00	0 0.00	1 0.10	
URINARY BLADDER	# EX 10	0	0	0	10
STOMACH	# EX 10	0	0	0	10
DUODENUM	# EX 10	0	0	0	10
ILEUM	# EX 10	0	0	0	10
CECUM	# EX 10	0	0	0	10

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: FEMALE

GROUP: NUMBER OF ANIMALS:	1		2		3		4	
	10	10	10	10	10	10	10	10
RECTUM	# EX	10	0	0	0	0	10	
MESENTERIC LYMPH NODE	# EX	10	0	0	0	0	10	
OVARIES	# EX	10	0	0	0	0	10	
UTERUS	# EX	10	0	0	0	0	10	
Dilatation, Bilateral		3 0.90	0 0.00	0 0.00	0 0.00	4 0.90		
SKIN	# EX	10	0	0	0	0	10	
CLITORAL GLANDS	# EX	10	0	0	0	0	10	
Lymphocytic Infiltrates		1 0.20	0 0.00	0 0.00	0 0.00	5 0.90		
Inflammation, Suppurative		0 0.00	0 0.00	0 0.00	0 0.00	1 0.20		
EYES	# EX	10	0	0	0	0	10	
Microgranuloma, Cornea		1 0.10	0 0.00	0 0.00	0 0.00	5 0.70		
HARDERIAN GLAND	# EX	10	0	0	0	0	10	
Lymphocytic Infiltrates		3 0.40	0 0.00	0 0.00	0 0.00	1 0.10		
FEMUR/STERNUM	# EX	10	0	0	0	0	10	
NASAL	# EX	10	0	0	0	0	10	
Inflammation, Subacute		0 0.00	0 0.00	0 0.00	0 0.00	1 0.10		
MAMMARY GLAND	# EX	10	0	0	0	0	10	

Severity Calculated by No. of Tissues Scored

(Report Continued)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP: NUMBER OF ANIMALS:	5		6		7		8	
	10		10		10		10	
BRAIN	# EX	10		0		0		10
NERVE	# EX	10		0		0		10
SPINAL CORD	# EX	10		0		0		10
SALIVARY GLAND	# EX	10		0		0		10
PANCREAS	# EX	10		0		0		10
Degeneration, Acinar		3 0.30		0 0.00		0 0.00		0 0.00
MANDIBULAR LYMPH NODE	# EX	10		0		0		10
ZYMBAL'S GLAND	# EX	9		0		0		10
PITUITARY	# EX	10		0		0		10
ADRENALS	# EX	10		0		0		10
THYROID	# EX	10		0		0		10
PARATHYROID	# EX	8		0		0		7
TRACHEA	# EX	10		0		0		10
ESOPHAGUS	# EX	10		0		0		10
THYMUS	# EX	10		2		1		10
Hemorrhage		3 0.40		2 2.00		1 1.00		4 0.60
HEART	# EX	10		0		0		10
Degeneration, Myocardial		0 0.00		0 0.00		0 0.00		1 0.20
Inflammation, Chronic		1 0.20		0 0.00		0 0.00		2 0.20
Inflammation, Chronic/Active, Arterial		0 0.00		0 0.00		0 0.00		1 0.10

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:	NUMBER OF ANIMALS:	5		6		7		8	
		10		10		10		10	
COLON		# EX	10		0		0		10
JEJUNUM		# EX	10		0		0		10
AORTA		# EX	10		0		0		10
LIVER		# EX	10		0		0		10
SPLEEN		# EX	10		10		10		10
Hyperplasia, Erythroid Cell			10 1.80		2 0.20		1 0.10		0 0.00
Pigmentation, NOS			4 0.40		0 0.00		0 0.00		0 0.00
Fibrosis			1 0.10		0 0.00		1 0.10		0 0.00
TONGUE		# EX	10		0		0		10
SKELETAL MUSCLE		# EX	10		0		0		10
LUNGS		# EX	10		0		0		10
Inflammation, Chronic			2 0.20		0 0.00		0 0.00		0 0.00
KIDNEYS		# EX	10		10		10		10
Mineralization, NOS			10 1.90		10 1.50		10 1.20		10 1.40
Pigmentation, Tubular Epithelium			10 1.90		1 0.10		0 0.00		0 0.00
Regeneration, Tubular			10 2.00		10 1.30		10 1.30		6 0.60
Cytoplasmic Droplets			10 2.90		10 2.00		0 0.00		0 0.00
Degeneration, Tubular			10 2.30		10 1.60		10 1.60		10 1.50
Hyaline Casts			9 1.00		0 0.00		0 0.00		0 0.00
URINARY BLADDER		# EX	10		0		0		10
Hemorrhage			3 0.30		0 0.00		0 0.00		0 0.00
PROSTATE		# EX	10		0		0		10
STOMACH		# EX	10		0		0		10

Severity Calculated by No. of Tissues Scored

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

SEVERITY SUMMARY

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

DAYS ON TEST: ALL

SEX: MALE

GROUP:

5

6

7

8

NUMBER OF ANIMALS:

10

10

10

10

DUODENUM

EX

10

SEV

0

SEV

0

SEV

10

ILEUM

EX

10

SEV

0

SEV

0

SEV

10

CECUM

EX

10

SEV

0

SEV

0

SEV

10

RECTUM

EX

10

SEV

0

SEV

0

SEV

10

MESENTERIC LYMPH NODE

EX

10

SEV

0

SEV

0

SEV

10

TESTES

EX

10

SEV

0

SEV

0

SEV

10

EPIDIDYMIDES

EX

10

SEV

0

SEV

0

SEV

10

SEMINAL VESICLE

EX

10

SEV

0

SEV

0

SEV

10

SKIN

EX

10

SEV

0

SEV

0

SEV

10

PREPUTIAL GLANDS

EX

10

SEV

0

SEV

0

SEV

10

Inflammation, Chronic/Active

1 0.20

SEV

0 0.00

SEV

0 0.00

SEV

3

0.60

Inflammation, Suppurative

2 0.20

SEV

0 0.00

SEV

0 0.00

SEV

0

0.00

Lymphocytic Infiltrates

4 0.40

SEV

0 0.00

SEV

0 0.00

SEV

3

0.30

EYES

EX

10

SEV

0

SEV

0

SEV

10

Microgranuloma, Cornea

3 0.30

SEV

0 0.00

SEV

0 0.00

SEV

4

0.50

HARDERIAN GLAND

EX

10

SEV

0

SEV

0

SEV

10

FEMUR/STERNUM

EX

10

SEV

0

SEV

0

SEV

10

Hyperplasia, Erythroid Cell

3 0.30

SEV

0 0.00

SEV

0 0.00

SEV

0

0.00

NASAL

EX

10

SEV

0

SEV

0

SEV

10

MAMMARY GLAND

EX

10

SEV

0

SEV

0

SEV

10

Severity Calculated by No. of Tissues Scored

(END OF REPORT)

091

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-001
 GROUP: 1
 SEX: FEMALE

ANIMAL ID:	01	02	03	04	05	06	07	08	09	10
BRAIN	N	N	N	N	N	N	N	N	N	N
NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	N	N	N	N	N	N	N	U	N
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
Hemorrhage	-	-	-	-	-	-	-	-	1	-
HEART	N	N	N	N	N	N	N	N	N	N
Inflammation, Chronic	1	-	-	-	-	-	-	-	-	-
COLON	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 1
SEX: FEMALE

ANIMAL ID:	01	02	03	04	05	06	07	08	09	10
JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N	N	N	N	N	N	N
Inflammation, Subacute	-	-	-	-	-	-	-	-	1	-
SPLEEN			N							N
Hyperplasia, Erythroid Cell	-	-	-	-	-	-	-	1	-	-
Pigmentation, NOS	2	1	-	1	1	1	2	-	2	-
Fibrosis	-	-	-	1	-	-	-	-	-	-
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS	N	N	N		N	N		N	N	N
Inflammation, Chronic	-	-	-	1	-	-	1	-	-	-
KIDNEYS										
Mineralization, NOS	1	1	1	-	1	1	1	1	2	1
Pigmentation, Tubular Epithelium	2	2	3	3	2	2	3	2	3	2
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 1

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	01	02	03	04	05	06	07	08	09	10
OVARIES	N	N	N	N	N	N	N	N	N	N
UTERUS	N		N		N	N	N	N	N	N
Dilatation, Bilateral	-	2	-	3	4	-	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
CLITORAL GLANDS	N	N	N	N		N	N	N	N	N
Lymphocytic Infiltrates	-	-	-	-	2	-	-	-	-	-
EYES	N		N	N	N	N	N	N	N	N
Microgranuloma, Cornea	-	1	-	-	-	-	-	-	-	-
HARDERIAN GLAND	N	N			N	N	N	N	N	
Lymphocytic Infiltrates	-	-	2	1	-	-	-	-	-	1
FEMUR/STERNUM	N	N	N	N	N	N	N	N	N	N
NASAL	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 2
SEX: FEMALE

ANIMAL ID: 11 12 13 14 15 16 17 18 19 20

BRAIN	*	*	*	*	*	*	*	*	*
NERVE	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*
HEART	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*
JEJUNUM	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 2
SEX: FEMALE

ANIMAL ID:	11	12	13	14	15	16	17	18	19	20
LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN	N	N	N					N	N	N
Pigmentation, NOS	-	-	-	-	1	1	1	-	-	-
Fibrosis	-	-	-	2	-	-	-	-	-	-
Depletion, Lymphoid	-	-	-	2	-	-	-	-	-	-
TONGUE	*	*	*	*	N	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	N	*	*	*	*	*
LUNGS	*	*	*	*	N	*	*	*	*	*
KIDNEYS										
Mineralization, NOS	-	1	1	1	1	1	1	1	1	1
Pigmentation, Tubular Epithelium	2	1	1	1	1	1	1	1	1	1
Regeneration, Tubular	-	-	-	-	-	-	-	-	-	1
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*
OVARIES	*	*	*	*	*	*	*	*	*	*
UTERUS	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-001

GROUP: 2

SEX: FEMALE

ANIMAL ID: 11 12 13 14 15 16 17 18 19 20

SKIN

* * * * * * * * * *

CLITORAL GLANDS

* * * * * * * * * *

EYES

* * * * * * * * * *

HARDERIAN GLAND

* * * * * * * * * *

FEMUR/STERNUM

* * * * * * * * * *

NASAL

* * * * * * * * * *

MAMMARY GLAND

* * * * * * * * * *

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 3

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	21	22	23	24	25	26	27	28	29	30
BRAIN	*	*	*	*	*	*	*	*	*	*
NERVE	*	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*	*
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-001

GROUP: 3

SEX: FEMALE

ANIMAL ID:	21	22	23	24	25	26	27	28	29	30
------------	----	----	----	----	----	----	----	----	----	----

LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN	N	N	N	N		N	N	N		N
Fibrosis	-	-	-	-	2	-	-	-	1	-
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNGS	*	*	*	*	*	*	*	*	*	*
KIDNEYS										
Mineralization, NOS	1	1	1	1	2	2	1	1	1	1
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*
OVARIES	*	*	*	*	*	*	*	*	*	*
UTERUS	*	*	*	*	*	*	*	*	*	*
SKIN	*	*	*	*	*	*	*	*	*	*
CLITORAL GLANDS	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-001

GROUP: 3

SEX: FEMALE

ANIMAL ID:	21	22	23	24	25	26	27	28	29	30
EYES	*	*	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*	*	*	*	*	*
NASAL	*	*	*	*	*	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*	*	*	*	*	*

/

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-001
 GROUP: 4
 SEX: FEMALE

ANIMAL ID:	31	32	33	34	35	36	37	38	39	40
------------	----	----	----	----	----	----	----	----	----	----

BRAIN	N	N	N	N	N	N	N	N	N	N
NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	N	U	N	N	N	N	N	N	U
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS Hemorrhage	-	-	-	-	1	-	1	1	-	-
HEART	N	N	N	N	N	N	N	N	N	N
Inflammation, Chronic	-	1	-	-	-	-	-	-	-	-
COLON	N	N	N	N	N	N	N	N	N	N
JEJUNUM	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 4

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	31	32	33	34	35	36	37	38	39	40
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N		N	N	N	N	N
Inflammation, Chronic	-	-	-	-	1	-	-	-	-	-
SPLEEN	N					N	N	N	N	N
Pigmentation, NOS	-	1	1	1	1	-	-	-	-	-
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS	N	N	N	N	N	N	N	N	N	N
Inflammation, Chronic	-	-	-	-	-	-	-	1	-	-
KIDNEYS									N	
Mineralization, NOS	2	1	2	1	1	2	1	1	-	1
Lymphocytic Infiltrates	-	-	-	1	-	-	-	-	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N	N	N	N	N	N
OVARIES	N	N	N	N	N	N	N	N	N	N
Cyst, NOS	-	P	-	-	-	-	-	-	-	-

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 4

DAYS ON TEST: ALL

SEX: FEMALE

ANIMAL ID:	31	32	33	34	35	36	37	38	39	40
------------	----	----	----	----	----	----	----	----	----	----

UTERUS			N	N		N	N	N	N	N
Dilatation, Bilateral	2	3	2	-	-	2	-	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
CLITORAL GLANDS	N					N	N	N	N	N
Lymphocytic Infiltrates	-	2	1	2	2	2	-	-	-	-
Inflammation, Suppurative	-	-	-	2	-	-	-	-	-	-
EYES			N	N	N			N	N	
Microgranuloma, Cornea	2	1	-	-	-	1	2	1	-	-
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
Lymphocytic Infiltrates	-	-	-	-	-	-	-	1	-	-
FEMUR/STERNUM	N	N	N	N	N	N	N	N	N	N
NASAL	N	N	N	N	N	N	N	N	N	N
Inflammation, Subacute	-	-	-	-	1	-	-	-	-	-
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(Report Continued)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-001
 GROUP: 5
 SEX: MALE

ANIMAL ID:	41	42	43	44	45	46	47	48	49	50
BRAIN	N	N	N	N	N	N	N	N	N	N
NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
Degeneration, Acinar	1	-	-	-	-	-	1	1	-	-
MANDIBULAR LYMPH NODE	N	N	N	N	N	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N	N	U	N	N	N
PITUITARY	N	N	N	N	N	N	N	N	N	N
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	N	N	U	N	N	N	U	N	N
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	N	N	N
Hemorrhage	-	1	-	-	-	-	-	2	1	
HEART	N	N	N	N	N	N	N	N	N	N
Inflammation, Chronic	-	-	-	-	2	-	-	-	-	-
COLON	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 5
SEX: MALE

ANIMAL ID:	41	42	43	44	45	46	47	48	49	50
------------	----	----	----	----	----	----	----	----	----	----

JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N	N	N	N	N	N	N
SPLEEN										
Hyperplasia, Erythroid Cell	1	2	2	2	2	2	1	2	2	2
Pigmentation, NOS	-	1	-	1	-	1	1	-	-	-
Fibrosis	-	-	-	-	-	-	-	-	1	-
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS	N	N	N	N	N	N	N	N	N	N
Inflammation, Chronic	1	-	-	-	-	-	-	1	-	-
KIDNEYS										
Mineralization, NOS	1	2	2	2	2	2	2	2	2	2
Pigmentation, Tubular Epithelium	2	2	2	2	1	2	2	2	2	2
Regeneration, Tubular	2	2	2	2	2	2	2	2	2	2
Cytoplasmic Droplets	3	3	3	3	3	3	3	3	2	3
Degeneration, Tubular	2	3	3	2	2	2	3	2	2	2
Hyaline Casts	1	1	-	1	1	1	1	2	1	1
URINARY BLADDER	N	N				N	N	N	N	N
Urolith, NOS	-	P	-	P	P	-	-	-	-	-
Hemorrhage	-	1	-	1	1	-	-	-	-	-
PROSTATE	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 5

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	41	42	43	44	45	46	47	48	49	50
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIDES	N	N	N	N	N	N	N	N	N	N
SEMINAL VESICLE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
PREPUTIAL GLANDS			N			N			N	
Inflammation, Chronic/Active	-	-	-	-	-	-	-	2	-	-
Inflammation, Suppurative	-	1	-	-	-	1	-	-	-	-
Lymphocytic Infiltrates	1	-	-	1	1	-	-	-	1	-
EYES	N	N			N	N	N	N	N	N
Microgranuloma, Cornea	1	-	-	1	1	-	-	-	-	-
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
FEMUR/STERNUM	N	N	N		N		N	N	N	N
Hyperplasia, Erythroid Cell	-	-	-	1	-	1	1	-	-	-
NASAL	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-001
 GROUP: 6
 SEX: MALE

ANIMAL ID:	51	52	53	54	55	56	57	58	59	60
------------	----	----	----	----	----	----	----	----	----	----

BRAIN	*	*	*	*	*	*	*	*	*	*
NERVE	*	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS Hemorrhage	-	-	-	-	-	2	-	-	-	2
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 6
SEX: MALE

ANIMAL ID:	51	52	53	54	55	56	57	58	59	60
LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN	N	N	N	N			N	N	N	N
Hyperplasia, Erythroid Cell	-	-	-	-	1	1	-	-	-	-
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNGS	*	*	*	*	*	*	*	*	*	*
KIDNEYS										
Mineralization, NOS	1	2	1	1	1	2	2	2	1	2
Pigmentation, Tubular Epithelium	1	-	-	-	-	-	-	-	-	-
Regeneration, Tubular	1	2	1	1	1	2	1	2	1	1
Cytoplasmic Droplets	2	2	2	2	2	2	2	2	2	2
Degeneration, Tubular	2	2	1	1	2	2	2	2	1	1
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
PROSTATE	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*
TESTES	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 6

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID: 51 52 53 54 55 56 57 58 59 60

EPIDIDYMIDES * * * * * * * * * *

SEMINAL VESICLE * * * * * * * * * *

SKIN * * * * * * * * * *

PREPUTIAL GLANDS * * * * * * * * * *

EYES * * * * * * * * * *

HARDERIAN GLAND * * * * * * * * * *

FEMUR/STERNUM * * * * * * * * * *

NASAL * * * * * * * * * *

MAMMARY GLAND * * * * * * * * * *

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-001
 GROUP: 7
 SEX: MALE

ANIMAL ID:	61	62	63	64	65	66	67	68	69	70
BRAIN	*	*	*	*	*	*	*	*	*	*
NERVE	*	*	*	*	*	*	*	*	*	*
SPINAL CORD	*	*	*	*	*	*	*	*	*	*
SALIVARY GLAND	*	*	*	*	*	*	*	*	*	*
PANCREAS	*	*	*	*	*	*	*	*	*	*
MANDIBULAR LYMPH NODE	*	*	*	*	*	*	*	*	*	*
ZYMBAL'S GLAND	*	*	*	*	*	*	*	*	*	*
PITUITARY	*	*	*	*	*	*	*	*	*	*
ADRENALS	*	*	*	*	*	*	*	*	*	*
THYROID	*	*	*	*	*	*	*	*	*	*
PARATHYROID	*	*	*	*	*	*	*	*	*	*
TRACHEA	*	*	*	*	*	*	*	*	*	*
ESOPHAGUS	*	*	*	*	*	*	*	*	*	*
THYMUS	*	*	*	*	*	*	*	*	*	*
Hemorrhage	-	-	-	-	-	1	-	-	-	-
HEART	*	*	*	*	*	*	*	*	*	*
COLON	*	*	*	*	*	*	*	*	*	*
JEJUNUM	*	*	*	*	*	*	*	*	*	*
AORTA	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-001
 GROUP: 7
 SEX: MALE

ANIMAL ID:	61	62	63	64	65	66	67	68	69	70
LIVER	*	*	*	*	*	*	*	*	*	*
SPLEEN	N	N	N	N	N	N		N	N	
Hyperplasia, Erythroid Cell	-	-	-	-	-	-	1	-	-	-
Fibrosis	-	-	-	-	-	-	-	1	-	-
TONGUE	*	*	*	*	*	*	*	*	*	*
SKELETAL MUSCLE	*	*	*	*	*	*	*	*	*	*
LUNGS	*	*	*	*	*	*	*	*	*	*
KIDNEYS										
Mineralization, NOS	1	1	1	1	2	1	2	1	1	1
Regeneration, Tubular	1	1	1	1	1	2	2	2	1	1
Degeneration, Tubular	1	1	2	2	2	2	2	2	1	1
URINARY BLADDER	*	*	*	*	*	*	*	*	*	*
PROSTATE	*	*	*	*	*	*	*	*	*	*
STOMACH	*	*	*	*	*	*	*	*	*	*
DUODENUM	*	*	*	*	*	*	*	*	*	*
ILEUM	*	*	*	*	*	*	*	*	*	*
CECUM	*	*	*	*	*	*	*	*	*	*
RECTUM	*	*	*	*	*	*	*	*	*	*
MESENTERIC LYMPH NODE	*	*	*	*	*	*	*	*	*	*
TESTES	*	*	*	*	*	*	*	*	*	*
EPIDIDYMIDES	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 7

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	61	62	63	64	65	66	67	68	69	70
SEMINAL VESICLE	*	*	*	*	*	*	*	*	*	*
SKIN	*	*	*	*	*	*	*	*	*	*
PREPUTIAL GLANDS	*	*	*	*	*	*	*	*	*	*
EYES	*	*	*	*	*	*	*	*	*	*
HARDERIAN GLAND	*	*	*	*	*	*	*	*	*	*
FEMUR/STERNUM	*	*	*	*	*	*	*	*	*	*
NASAL	*	*	*	*	*	*	*	*	*	*
MAMMARY GLAND	*	*	*	*	*	*	*	*	*	*

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 8

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	71	72	73	74	75	76	77	78	79	80
BRAIN	N	N	N	N	N	N	N	N	N	N
NERVE	N	N	N	N	N	N	N	N	N	N
SPINAL CORD	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
MANDIBULAR LYMPH NODE	N	N	N	N	N	N	N	N	N	N
ZYMBAL'S GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY Cyst, NOS, Pars Distalis	-	-	-	-	-	-	-	P	-	-
ADRENALS	N	N	N	N	N	N	N	N	N	N
THYROID	N	N	N	N	N	N	N	N	N	N
PARATHYROID	N	N	N	N	U	N	U	N	U	N
TRACHEA	N	N	N	N	N	N	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
THYMUS Hemorrhage	-	1	-	-	2	1	-	-	2	-
HEART Degeneration, Myocardial	-	-	-	-	-	-	-	-	-	2
Inflammation, Chronic	1	-	-	-	1	-	-	-	-	-
Inflammation, Chronic/Active, Arter	-	-	-	-	-	1	-	-	-	-
COLON	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 8

DAYS ON TEST: ALL

SEX: MALE

ANIMAL ID:	71	72	73	74	75	76	77	78	79	80
JEJUNUM	N	N	N	N	N	N	N	N	N	N
AORTA	N	N	N	N	N	N	N	N	N	N
LIVER	N	N	N	N	N	N	N	N	N	N
SPLEEN	N	N	N	N	N	N	N	N	N	N
TONGUE	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
LUNGS	N	N	N	N	N	N	N	N	N	N
KIDNEYS										
Mineralization, NOS	1	2	2	1	2	1	1	1	2	1
Regeneration, Tubular	-	1	1	-	1	1	-	-	1	1
Degeneration, Tubular	1	2	2	1	2	1	1	1	2	2
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
Urolith, NOS	-	-	-	-	-	-	-	P	-	-
PROSTATE	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
DUODENUM	N	N	N	N	N	N	N	N	N	N
ILEUM	N	N	N	N	N	N	N	N	N	N
CECUM	N	N	N	N	N	N	N	N	N	N
RECTUM	N	N	N	N	N	N	N	N	N	N
MESENTERIC LYMPH NODE	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

TABULATED ANIMAL DATA

STUDY ID : 90 Day Tetryl
 FATE: ALL
 DAYS ON TEST: ALL

STUDY NUMBER: 94-001
 GROUP: 8
 SEX: MALE

ANIMAL ID:	71	72	73	74	75	76	77	78	79	80
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIDES	N	N	N	N	N	N	N	N	N	N
SEMINAL VESICLE	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N
PREPUTIAL GLANDS	N	N		N			N			
Inflammation, Chronic/Active	-	-	2	-	-	2	-	-	-	2
Lymphocytic Infiltrates	-	-	-	-	1	-	-	1	1	-
EYES		N		N			N	N	N	N
Microgranuloma, Cornea	1	-	2	-	1	1	-	-	-	-
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
FEMUR/STERNUM	N	N	N	N	N	N	N	N	N	N
NASAL	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

(END OF REPORT)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 1
SEX: FEMALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 2
SEX: FEMALE

No Gross Observations for any animal in this group

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-001

GROUP: 3

SEX: FEMALE

No Gross Observations for any animal in this group

(REPORT CONTINUED)

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl

FATE: ALL

DAYS ON TEST: ALL

STUDY NUMBER: 94-001

GROUP: 4

SEX: FEMALE

Animal ID: 32

Pathologist: GRO

Animal Fate: Terminal Sacrifice

Days on Test: 90

Reference to Necropsy Record:

OVARIES - Unilateral, Right, Cyst, 8mm in Diameter,
(1), Round, Red

Related Histopathology:

OVARIES - Cyst, NOS

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 5
SEX: MALE

No Gross Observations for any animal in this group

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 6

DAYS ON TEST: ALL

SEX: MALE

Animal ID: 56

Pathologist: GRO

Animal Fate: Terminal Sacrifice

Days on Test: 90

Reference to Necropsy Record:

Related Histopathology:

THYMUS - Discolored, Red, Moderate

THYMUS - Hemorrhage

Animal ID: 60

Pathologist: GRO

Animal Fate: Terminal Sacrifice

Days on Test: 90

Reference to Necropsy Record:

Related Histopathology:

THYMUS - Foci, 1mm in Diameter, >5, Red

THYMUS - Hemorrhage

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl

STUDY NUMBER: 94-001

FATE: ALL

GROUP: 7

DAYS ON TEST: ALL

SEX: MALE

Animal ID: 66

Pathologist: GRO

Animal Fate: Terminal Sacrifice

Days on Test: 90

Reference to Necropsy Record:

Related Histopathology:

THYMUS - Discolored, Pinpoint, Multiple (>5), Red,
Spots

THYMUS - Hemorrhage

Pathology Associates, Inc.
Study Number 94-001
90 Day Tetryl Exposure
in Fischer 344 Rats

CORRELATION OF GROSS & MICRO

STUDY ID : 90 Day Tetryl
FATE: ALL
DAYS ON TEST: ALL

STUDY NUMBER: 94-001
GROUP: 8
SEX: MALE

Animal ID: 79
Animal Fate: Terminal Sacrifice

Pathologist: GRO
Days on Test: 90

Reference to Necropsy Record:
THYMUS - Discolored, Multiple, Red, Spots

Related Histopathology:
THYMUS - Hemorrhage

APPENDIX H

OPHTHALMOLOGY

DATA

Ophthalmology Report

David A. Wilkie DVM, MS
Diplomate ACVO

Introduction

The following are results of ocular examinations. All ocular examinations were performed by a Board-Certified Veterinary Ophthalmologist.

Materials and Methods

A preliminary ophthalmic examination was performed on the eyes of all rats by Dr David Wilkie DVM, MS, Dip. ACVO prior to initiation of the study. Examinations included:

1. Biomicroscopic examination, using a Zeiss HSO-10 biomicroscope, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).
2. Indirect ophthalmoscopic examination, using a 30 diopter lens, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).

Results

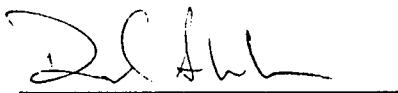
Initial Examination

Corneal dystrophy (crystals) -

The eyes of all animals examined were affected by corneal dystrophy/crystals. All animals were affected with mild corneal dystrophy OU.

Conclusions

All animals to be used in this study are affected with mild corneal dystrophy prior to the initiation of the study. Corneal dystrophy is a common finding in Fisher 344 rats of both sexes. In a 90 day study such as this the corneal lesions should not progress significantly and do not interfere with examination of the intraocular tissues.



Date: 1/16/94

David A. Wilkie DVM, MS
Diplomate ACVO
Assistant Professor
Department of Veterinary Clinical Sciences
The Ohio State University
1935 Coffey Road
Columbus, Ohio 43210

Ophthalmology Report

David A. Wilkie DVM, MS
Diplomate ACVO

Introduction

The following are results of ocular examinations. All ocular examinations were performed by a Board-Certified Veterinary Ophthalmologist.

Materials and Methods

A final ophthalmic examination was performed on the eyes of all rats by Dr David Wilkie DVM, MS, Dip. ACVO prior to completion of the study. Examinations included:

1. Biomicroscopic examination, using a Zeiss HSO-10 biomicroscope, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).
2. Indirect ophthalmoscopic examination, using a 30 diopter lens, following dilation of the pupils with 1.0% tropicamide (Mydriacyl®).

ResultsInitial Examination

Corneal dystrophy (crystals) -

The eyes of all animals examined were affected by corneal dystrophy/crystals. All animals were affected with mild corneal dystrophy OU with the exception of the right eye of animal #46 where the corneal dystrophy was moderate in severity.

Conjunctivitis (mild) -

Mild conjunctivitis was noted in animal #80 and involved the left eye.

Conclusions

All animals used in this study were affected with mild corneal dystrophy prior to the initiation of the study. Corneal dystrophy is a common finding in Fisher 344 rats of both sexes. With the exception of animal #46 the corneal dystrophy has not progressed. The conjunctivitis noted in animal #80 is an incidental finding. There is no treatment or group effect observed.



Date: 4/13/94

David A. Wilkie DVM, MS
Diplomate ACVO
Assistant Professor
Department of Veterinary Clinical Sciences
The Ohio State University
1935 Coffey Road
Columbus, Ohio 43210

APPENDIX I

CHEMICAL ANALYSES

Determination of Homogeneity
of Tetryl in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 1				
3000	Top	2880	2830	2.03
	Middle	2780		1.62
	Bottom	2810		0.41
1000	Top	1100	1070	2.60
	Middle	1080		0.51
	Bottom	1040		3.11
200	Top	207	194	6.75
	Middle	184		5.36
	Bottom	191		1.39
WEEK 2				
3000	Top	2720	2720	0.00
	Middle	2730		0.28
	Bottom	2710		0.29
1000	Top	920	960	4.39
	Middle	1020		5.83
	Bottom	950		1.43
200	Top	207	200	3.43
	Middle	192		3.92
	Bottom	201		0.49

Determination of Homogeneity
of Tetryl in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 3				
3000	Top	2920		4.69
	Middle	2700	2790	3.29
	Bottom	2750		1.40
1000	Top	990		4.94
	Middle	1050	1040	0.94
	Bottom	1080		3.99
200	Top	192		2.14
	Middle	188	196	4.12
	Bottom	209		6.25
WEEK 4				
3000	Top	3190		2.25
	Middle	3110	3120	0.40
	Bottom	3060		1.86
1000	Top	950		0.09
	Middle	960	950	1.11
	Bottom	940		1.02
200	Top	199		1.68
	Middle	207	203	2.43
	Bottom	201		0.75

Determination of Homogeneity
of Tetryl in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 5				
3000	Top	3190	2910	9.42
	Middle	2820		3.35
	Bottom	2740		6.06
1000	Top	1080	1040	3.82
	Middle	1020		1.39
	Bottom	1010		2.43
200	Top	188	185	1.53
	Middle	185		0.15
	Bottom	182		1.68
WEEK 6				
3000	Top	2780	2830	1.91
	Middle	2890		1.85
	Bottom	2830		0.06
1000	Top	890	930	4.72
	Middle	920		1.13
	Bottom	990		5.85
200	Top	192	190	0.85
	Middle	184		3.52
	Bottom	195		2.67

Determination of Homogeneity
of Tetryl in the diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 7				
3000	Top	2810		1.45
	Middle	2770	2770	0.01
	Bottom	2730		1.46
1000	Top	940		2.13
	Middle	880	920	3.80
	Bottom	930		1.67
200	Top	194		3.97
	Middle	184	186	1.44
	Bottom	182		2.52
WEEK 8				
3000	Top	2970		5.29
	Middle	3270	3130	4.32
	Bottom	3160		0.97
1000	Top	940		1.45
	Middle	980	950	2.57
	Bottom	940		1.13
200	Top	205		2.82
	Middle	210	211	0.21
	Bottom	217		3.03

Determination of Homogeneity
of Tetryl in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 9				
3000	Top	3380		5.60
	Middle	3240	3200	1.42
	Bottom	2970		7.03
1000	Top	1070		0.24
	Middle	1060	1070	1.13
	Bottom	1080		0.88
200	Top	210		2.09
	Middle	200	200	2.99
	Bottom	200		0.90
WEEK 10				
3000	Top	2930		7.83
	Middle	2570	2720	5.46
	Bottom	2650		2.37
1000	Top	880		11.39
	Middle	1140	1000	14.66
	Bottom	960		3.27
200	Top	180		0.53
	Middle	200	180	10.00
	Bottom	160		10.54

Determination of Homogeneity
of Tetryl in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 11				
3000	Top	3160		0.51
	Middle	3200	3180	0.64
	Bottom	3180		0.13
1000	Top	1030		1.91
	Middle	960	1010	4.76
	Bottom	1030		2.85
200	Top	192		1.82
	Middle	195	195	0.05
	Bottom	199		1.86
WEEK 12				
3000	Top	2810		4.91
	Middle	2850	2960	3.56
	Bottom	3210		8.41
1000	Top	1020		0.83
	Middle	1040	1010	2.71
	Bottom	970		3.53
200	Top	218		6.15
	Middle	205	206	0.26
	Bottom	193		5.89

Determination of Homogeneity
of Tetryl in the Diet

Target Concentration (mg/kg diet)	Site of Sampling	Concentration by Analysis (mg/kg diet)	Mean Concentration (mg/kg diet)	Deviation from Mean (%)
WEEK 13				
3000	Top	3160		0.24
	Middle	3150	3150	0.15
	Bottom	3150		0.09
1000	Top	990		2.35
	Middle	980	960	1.65
	Bottom	920		4.00
200	Top	203		4.66
	Middle	188	194	3.13
	Bottom	191		1.53

Analysis of Tetryl
in the Feed Mixtures

Target Concentration (mg/kg diet)	Date Prepared	Date Analyzed	Concentration by Analysis (mg/kg diet)	% Error
Week 1				
3000	4 Jan 94	7 Jan 94	2830	5.81
1000	5 Jan 94	7 Jan 94	1070	7.49
200	6 Jan 94	10 Jan 94	194	2.96
Week 2				
3000	11 Jan 94	21 Jan 94	2720	9.34
1000	12 Jan 94	26 Jan 94	960	3.71
200	13 Jan 94	25 Jan 94	200	0.16
Week 3				
3000	18 Jan 94	26 Jan 94	2790	6.96
1000	20 Jan 94	27 Jan 94	1040	3.76
200	21 Jan 94	27 Jan 94	196	1.86
Week 4				
3000	24 Jan 94	2 Feb 94	3120	4.01
1000	24 Jan 94	2 Feb 94	950	5.26
200	25 Jan 94	2 Feb 94	203	1.28
Week 5				
3000	31 Jan 94	4 Feb 94	2910	2.84
1000	1 Feb 94	8 Feb 94	1040	3.60
200	2 Feb 94	9 Feb 94	184	7.51

Analysis of Tetryl
in the Feed Mixtures

Target Concentration (mg/kg diet)	Date Prepared	Date Analyzed	Concentration by Analysis (mg/kg diet)	% Error
Week 6				
3000	7 Feb 94	16 Feb 94	2830	5.56
1000	8 Feb 94	17 Feb 94	930	6.54
200	9 Feb 94	17 Feb 94	190	4.84
Week 7				
3000	14 Feb 94	24 Feb 94	2770	7.76
1000	16 Feb 94	1 Mar 94	920	8.17
200	17 Feb 94	1 Mar 94	186	6.79
Week 8				
3000	22 Feb 94	3 Mar 94	3130	4.43
1000	23 Feb 94	4 Mar 94	950	4.76
200	24 Feb 94	4 Mar 94	211	5.38
Week 9				
3000	28 Feb 94	9 Mar 94	3200	6.65
1000	2 Mar 94	10 Mar 94	1070	7.14
200	3 Mar 94	11 Mar 94	200	1.37
Week 10				
3000	7 Mar 94	14 Mar 94	2720	9.43
1000	10 Mar 94	14 Mar 94	1000	0.30
200	11 Mar 94	17 Mar 94	180	9.23

Analysis of Tetryl
in the Feed Mixtures

Target Concentration (mg/kg diet)	Date Prepared	Date Analyzed	Concentration by Analysis (mg/kg diet)	% Error
Week 11				
3000	14 Mar 94	18 Mar 94	3180	6.02
1000	15 Mar 94	23 Mar 94	1010	0.63
200	17 Mar 94	24 Mar 94	195	2.44
Week 12				
3000	21 Mar 94	24 Mar 94	2960	1.43
1000	23 Mar 94	24 Mar 94	1010	0.83
200	24 Mar 94	30 Mar 94	206	2.79
Week 13				
3000	28 Mar 94	31 Mar 94	3150	5.11
1000	28 Mar 94	1 Apr 94	960	3.76
200	29 Mar 94	7 Apr 94	194	2.81

APPENDIX J

**PROTOCOL AND
AMENDMENTS**

PROTOCOL

90-Day Subchronic Toxicity Evaluation of N-Methyl-N,2,4,6-Tetranitroaniline in Male and Female Fischer (F344) Rats

This study will be conducted in agreement with Good Laboratory Practice Standards, Environmental Protection Agency, Toxic Substances Control Act (TSCA) 40 CFR Part 792 (Federal Register, Vol 54, No. 158, August 17, 1989, pp. 34034 - 34050). All aspects of the studies will be conducted in accordance with written Standard Operating Procedures (SOP) of the performing unit and all raw data and performance documents will be maintained in agreement with GLP. An administratively separate quality assurance unit (QAU from PAI) will monitor the studies to assure adherence to good laboratory practices and the approved SOPs. Any deviation from the protocol or GLP will be noted in the raw data and reflected in the final report.

Testing Facility
A.W. Breidenbach Environmental Research Center
U.S. Environmental Protection Agency
Cincinnati, OH 45268

Prime Contractor (Sponsor)
U.S. Army Biomedical Research and
Development Laboratory, Fort Detrick
Frederick, Maryland 21701-5010

T. V. Reddy 12-15-93
Principal Investigator Date
T.V. Reddy, Ph.D.

G. Reddy 12-27-93
G. Reddy, Ph.D., Sponsor Date

A. R. Olson 12/15/93
Project Manager Date
G.R. Olson, DVM, Ph.D.
Pathology Associates, Inc.

W.R. Fox 12-15-93
Quality Assurance Date
W.R. Fox, MA
Pathology Associates, Inc.

90-DAY SUBCHRONIC TOXICITY EVALUATION OF
N-METHYL-N,2,4,6-TETRANITROANILINE
IN MALE AND FEMALE FISCHER (F344) RATS

RESEARCH PROTOCOL

Tirumuru V. Reddy, Ph.D.
Principal Investigator

F. Bernard Daniel, Ph.D.
Co-Principal Investigator

Ecological Monitoring Research Division
Environmental Monitoring Systems Laboratory - Cincinnati
U.S. Environmental Protection Agency
Cincinnati, Ohio 45268

December 15, 1993

TITLE: 90-DAY SUBCHRONIC TOXICITY EVALUATION OF N-METHYL-N,2,4,6-TETRANITROANILINE IN MALE AND FEMALE FISCHER (F344) RATS

BACKGROUND:

Nitroaromatics, such as 1,3-dinitrobenzene (DNB), 1,3,5-trinitrobenzene (TNB), and N-methyl-N,2,4,6-tetranitroaniline (tetryl), have been detected as environmental contaminants of groundwater and soil near production sites and in some instances at military test grounds. The wastewaters discharged from trinitrotoluene (TNT) manufacturing processes contain a variety of aromatic compounds, including DNB and TNB. TNB is formed during the nitration step of TNT synthesis as a result of oxidation of methyl groups. Although the complete mechanism of TNB formation during TNT photolysis is unknown, Burlinson (1980) suggested that it is produced by decarboxylation of 2,4,6-trinitrobenzaldehyde, a major TNT photoproduct. It is also found in aquatic systems and surface soils as a by-product of photolysis of TNT. DNB and TNB are not easily biodegradable, persist in the environment, eventually leach out, and contaminate groundwater near waste disposal sites. Tetryl is an explosive that has been in use, largely for military purposes, since 1906. Wastewaters and soil at the original production sites and other plants devoted to munitions assembly, contain large quantities of tetryl. A recent estimate of tetryl in wastewaters generated from the production of tetryl at Joliet Army Ammunition Plant was about 36 lb/per day of each production line.

Toxicity data on these compounds are limited. The oral LD₅₀ of DNB, TNB and tetryl were 59 mg/kg, 284 mg/kg and greater than 5 g/kg, respectively, in rats for combined sexes. TNB and tetryl were not toxic at 2 g/kg when applied to rabbit skin for 24 hours. However, the dermal LD₅₀ of DNB was 1.99 g/kg for combined sexes of rabbits. None of these compounds produced skin irritation potentials but positive (DNB) and severe (TNB, tetryl) eye irritation potentials in rabbits. The sensitization tests showed that DNB and tetryl are not skin sensitizers while TNB caused mild allergic reaction in guinea pigs. Some of the toxicological and behavioral effects of DNB are; formation of methemoglobin, testicular degeneration and reproductive failure, and weight loss and anemia in hamsters, rats and mice. Neurological and hematological disorders have also been reported in dogs. DNB is rather toxic to humans; the estimated lethal dose range is 5-50 mg/kg. It is readily absorbed through the skin. Fetal doses (amount and route of administration are not given) of tetryl produced toxic degeneration (necrosis) in the kidneys of dogs and rabbits and liver necrosis in dogs (not in rabbits). Tetryl was observed to be a powerful skin sensitizer in ammunition plant workers. Hardy and Maloof (1950) reported effects from accidental exposure of 11 people to tetryl: two died, one was disabled and eight did not detect permanent disability. They also reported irreversible liver damage, dermatitis, and upper respiratory irritation following tetryl exposure. The effects of tetryl exposure include gastrointestinal symptoms and epidermal, respiratory, nervous system, hematopoietic and circulatory injury. Atmospheric concentration of 1.5 mg/m³ or below did not produce systemic poisoning in persons working with tetryl. DNB, TNB, and tetryl have been shown to be genotoxic in *Salmonella* mutagenesis assay. TNB has been shown to form adducts of blood proteins and tissue DNA in rats.

PROTOCOL

1. Study. 90-day Subchronic toxicity evaluation with N-Methyl-N,2,4,6-tetranitroaniline (tetryl) in F344 male and female rats.
2. Purpose. To evaluate subchronic toxicity of tetryl when administered in the diet for 90-days.
3. Study Location. Andrew W. Breidenbach Environmental Research Center, U.S. Environmental Protection Agency, Cincinnati, OH 45268
4. Sponsor and Address. U.S. Army Biomedical Research and Development Laboratory, Fort Detrick, Frederick, Maryland 21701-5010
5. Principle Investigator. T.V. Reddy, Ph.D., Research Chemist Environmental Monitoring Systems Laboratory, U.S. Environmental Protection Agency, Cincinnati, Ohio 45268
6. Co-Principle Investigator. F. Bernard Daniel, Ph.D, Environmental Monitoring Systems Laboratory, U.S. Environmental Protection Agency, Cincinnati, Ohio 45268
7. Study Coordinator. Barry Wiechman, MS., Pathology Associates (ROW)
8. Project Manager. G.R. Olson, DVM, Ph.D., Pathology Associates (PAI)
9. Regulatory Compliance. This study is carried out according to U.S. EPA Health Effects testing guidelines (40 CFR 798) in compliance with GLP (40 CFR 792)
10. Quality Assurance. The protocol in life phase and final report will be audited by the Quality Assurance Office in accordance with SOP's at Pathology Associates, West Chester, Ohio 45069.
11. Test Material. N-Methyl-N,2,4,6-tetranitroaniline (tetryl) (CAS#479-45-8) is supplied by the U.S. Army Biomedical Research and Development Laboratory, Ft. Detrick, Frederick, Maryland 21702. The sponsor will be responsible for the purity of the test chemical.
:
12. Experimental Design.
 - A. Selection of Dose: An appropriate dose will be selected from 14-day range finding study. Toxikon Corporation, Woburn, MA 01801 has conducted acute toxicity studies on Tetryl. They administered Tetryl in corn oil to

rats at a single oral (Bolus) dose and observed the clinical signs for 14 days following dosing. They have reported that tetryl is nontoxic even at dose levels of 5 g/kg B.W. No unusual lesions were reported at necropsy in male and female rats. There were no established reports on the LD50 values. There are no reports on the chronic effects of tetryl in rats. Therefore, a pilot study is designed to determine the palatability.

B. Preparation of the Diet: Certified powdered Purina laboratory chow purchased from Purina labs and stored at 4°C is used. Analysis of the feed for each batch is supplied by the manufacturer. Feed analysis data suggests that the contaminants reported in feed do not have adverse effects on the test. Tetryl diets are prepared once a week. Just before the diet preparation, tetryl is removed from the storage shelves (kept in designated carcinogen room), weighed in the carcinogen room and mixed with the powdered diet (10g/kg/diet g/kg). First, 10g tetryl granules are powdered by grinding in a pestle and mortar and then mixed with 250g powdered diet and mixed for 15 min. Then an additional 250 g of powdered diet is added and mixed for an additional 15 min. Then the remaining diet will be added to bring the tetryl concentration to 10 g/kg; then mixed for an additional hour in a mechanical stirrer (Kitchen Aid heavy duty stand mixer, Model No. K5SS) for uniform distribution of tetryl in the diet. This is also verified by determining the tetryl concentration in the diet taken from three different depths (top, middle and bottom layer) of the mixing chamber. Quantitative analysis of tetryl is done by HPLC.

The premixed diet (10 g/kg) is further diluted with fresh powdered diet to obtain the desired tetryl concentration in the diet as determined from 1x day range finding study. Individual diet concentrations are determined as described before. Tetryl concentrations are manipulated in such a way that each rat (caged individually) will receive the desired amount of tetryl. This is determined by calculating the daily average intake, followed by an adjustment of tetryl content in the diet. Dietary intake and water consumption are measured twice a week. Body weights are recorded once a week.

C. Animal Husbandry: Animals will be housed 2 per cage in suspended stainless steel cages. All housing and care will be carried out according to the standards recommended by the Guide for the Care of Laboratory Animals (DHHS Publication No. (NIH) 86-23, 1989).

D. Randomization: Using computer-generated random numbers with assignment to groups. At the time of randomization, the weight variation of the animals of each sex used should not exceed \pm 2 SD of the mean weight, and the mean body weights for each group of each sex will not be statistically different.

E. Justification: Rats (6-8 weeks old) historically have been used in safety evaluation studies and are recommended by appropriate regulatory agencies.

F. Test Species: Fisher 344 rats (50 male and 50 female, 6-7 weeks old) will be obtained from the Charles River Labs, Inc., Portage, MI. All

animal identification is made by using electronic implants. Cage cards and diet preparations will be color-coded by dose groups. Distilled water will be provided *ad libitum* using water bottles with stainless double ball sipper tabs. Upon arrival, the animals will be quarantined for one week. During the quarantine period, the animals will be observed for fitness and serology tests will be performed. Animals with any pathological signs will not be included in the study.

G. Group designation and dose levels for 90-day toxicity study:

Group	No. of Rats	Sex	Tetryl Conc. in the Diet g/kg	Tetryl mg/kg/diet	Sacrifice Time (days)
1	10	Male	0	0	90
2	10	"	A*	3000	90
3	10	"	B	1000	90
4	10	"	C	200	90
5	10	Female	0	0	90
6	10	"	A	3000	90
7	10	"	B	1000	90
8	10	"	C	200	90

*A, b, c will be determined from 90 day range finding study.

H. Analysis of the Diet: The stability and the homogeneity of tetryl in the diet is determined by analyzing the tetryl content (by HPLC) in the diet, soon after diet preparation and after each feeding intervals.

I. Observation of Animals:

(1) Clinical Observations:

Twice daily - mortality and morbidity check.

Once daily - cageside observation for obvious indications of a toxic effect; these effects will be recorded as they are observed.

Data for mortality and morbidity checks and cageside observations will be recorded on the same form. Because these are cageside animal checks, the observations will not be as specific and may not necessarily duplicate those observations recorded on body weight days when thorough physical examinations are conducted.

(2) Physical Examinations: At each weighing interval - These observations will include, but not be limited to, changes in: skin and

fur; eyes and mucous membranes; respiratory, circulatory, autonomic and central nervous systems; some motor activity and behavior.

- (3) Body Weight: Prior to treatment and weekly, thereafter.
- (4) Food Consumption: Weekly - twice.
- (5) Water Consumption: Weekly - twice.
- (6) Ophthalmoscopic examination: Prior to the treatment and the termination by a board certified veterinarian

J. Clinical Pathology:

- (1) Frequency: At termination.
- (2) Number of Animals: All animals.

K. Tests:

(1) Hematology:

leukocyte count	methemoglobin
erythrocyte count	hematocrit
heinz bodies	platelet count
hemoglobin	differential leukocyte count

(2) Blood Chemistry:

glucose	urea nitrogen
sodium	creatinine
potassium	aspartate aminotransferase
total protein	alanine aminotransferase
albumin - phosphorus	alkaline phosphatase
calcium	
total bilirubin	

L. Termination:

(1) Unscheduled Sacrifices and Deaths: Necropsies, by trained personnel using procedures approved by board-certified pathologists, will be conducted on all moribund animals and on all animals that die.

(2) Sacrifice: After 90 days of treatment, all surviving animals will be weighed, anesthetized with sodium pentobarbital, and exsanguinated. Necropsies will be conducted on each animal in a random order to eliminate bias by trained personnel using procedures approved by board-certified pathologists. Animals will be fasted for 12 hrs before sacrifice.

A pathologist will be readily available for consultation (further participation by a pathologist is available).

M. Postmortem Procedures:

(1) Gross Necropsy: The necropsy will include examination of:

external surface
all orifices
cranial cavity
carcass
external surface of the brain (at necropsy) - cut surfaces of the brain
thoracic, abdominal and pelvic cavities and their viscera
cervical tissues and organs

(2) Organ Weights: For each terminally sacrificed animal, the following organs (when present) will be weighed following careful dissection and trimming to remove fat and other contiguous tissue in a uniform manner:

brain	lungs
liver	thymus
spleen	testes with epididymides/ovaries
kidneys	heart
adrenals	

(3) Tissue Preservation: The following tissues (when present) from each animal will be preserved in 10% neutral buffered formalin:

skin	ileum
mandibular lymph nodes	colon
mesenteric lymph nodes	cecum
mammary glands	rectum
thigh muscle	liver
sciatic nerve	pancreas
sternum with marrow	spleen
femur with marrow	kidneys
larynx	adrenals
thymus	urinary bladder
trachea	seminal vesicles
lungs and bronchi	prostate
heart and aorta	testes, including epididymis
thyroid	ovaries
parathyroids	uterus
esophagus	nasal cavity and nasal turbinates
stomach	brain
duodenum	pituitary
jejunum	preputial or clitoral glands
tongue	Zymbal's gland
salivary gland	thoracic spinal cord

N. Histopathology:

(1) Following necropsy, a list of all gross lesions recorded will be submitted to the project officer at U.S. Army Biomedical Research and Development Laboratory for his evaluation and for any additional

histopathology other than those described below.

Histopathological evaluations are to be done on the following tissues from all the animals (male and female from the highest dose group and untreated controls). The tissues examined under a light microscope are as follows:

cerebrum	pancreas
cerebellum	cecum
trachea	colon
thyroid	rectum
parathyroid	stomach
esophagus	skeletal muscle
salivary gland	sciatic nerve
harderian gland	tongue
heart	skin
aorta	mammary gland
lung	nasal region
thymus	sternum
spleen	femur
mesenteric lymph node	vertebrae
liver	spinal cord
kidneys	adrenals
urinary bladder	pituitary
duodenum	eye(s)
jejunum	Zymbal's gland
ileum	

MALE

accessory sex glands
epididymis
testes

FEMALE

uterus
ovaries

An average of 12 slides will be prepared for each rat covering all the tissues shown above (3 or 4 tissues are fixed on each slide). A total of 480 slides from 40 rats(10 male and 10 female from high dose control group) from the 14-day study will be examined. Based on the results from high dose group tissues from other doses, groups will be examined as needed. Following completion of each study, all wet tissues, paraffin blocks and slides will be placed in the EPA storage facility.

O. Final Report:

Two months after the termination of the in-life phase of the study, eight copies of the final report which includes the following information (as appropriate) will be prepared and submitted to the project officer at EPA. Appropriate records are maintained during the test period and returned to the project officer at the completion.

(1) Experimental Design and Methods:

(2) Results:

mortality
clinical observations
body weights
food and liquid consumption
clinical pathology tests

organ weights and organ/body
weight ratios
gross pathology
histopathology

Statistical Evaluation:

Stat-view computer software will be used for statistical analysis.

Dunnet's t-test will be used for comparing the treatment groups.

Kruskal-Wallis rank sums will be used, if needed, to examine the differences among the treatment groups and Wilcoxon rank sum test will be used to analyze pairwise differences between the control and each dose group.

- P. Proposed starting date: January 1994
- Q. Proposed termination date: March 1994
- R. Proposed draft report: June 1994
- S. Final Report due: July 1994.

Amendment 1
for
United States Army Study 94-001
SUBCHRONIC TOXICITY EVALUATION OF N-METHYL-N, 2,4,6-TETRANITROANILINE IN FISCHER (F344) RATS

For
United States Army
Biomedical Research and Development Laboratory
Fort Detrick
Frederick, MD 21701-5010

The purpose of Amendment 1 is provide data for hematology and clinical chemistries at 45 days.

1. Page 6, add the following:

J. Clinical Pathology
(1) Frequency: At 45 days and termination.

Reason: This statement was incorrect in the original protocol.

Amendment 1 Approval

U.S. Army Medical Research and
Development Laboratory
Fort Detrick
Frederick, Maryland 21701-5010

AW Breidenbach Environmental
Research Center
U.S. Environmental Protection Agency
Cincinnati, Ohio 45268

Gundreddy 10-27-94 T.V. Reddy 10.14.94
G. Reddy, Ph.D., Sponsor Date T.V. Reddy, Ph.D., PI Date

Willa Fox Willa Fox 9-7-94
Willa Fox, MA, QA Date

Deviations from GLP's and Protocol

1. Clinical observations were performed twice daily but recorded once daily.
2. The mandibular lymph node and preputial glands were histopathologically examined while the vertebrae were not.
3. A portion (2 grams) of the median lobe was removed after weighing and frozen in liquid nitrogen for biochemical analysis.

Tirumuru V. Reddy

Tirumuru V. Reddy, Ph.D.

DISTRIBUTION LIST

Commander
ATTN: SGRD-UBZ-C
U.S. Army Biomedical Research and Development Laboratory
Fort Detrick, Frederick, MD 21702-5010

Commander
ATTN: MCMR-RMI-S
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, MD 21702-5012

Commander/Director
U.S. Army Corps of Engineers
Construction Engineering Research Laboratory
Environmental Division
P.O. Box 4005
Champaign, IL 61820

Commandant
Academy of Health Sciences, U.S. Army
ATTN: DRXTH-ES
Aberdeen Proving Ground, MD 21010-5000

Commander
U.S. Army Environmental Hygiene Agency
ATTN: Library
Aberdeen Proving Ground, MD 21020-5000

Commander
U.S. Army Environmental Center
ATTN: S-FIM-AEC-TSS (Mr. R. L. Muhly)
Aberdeen Proving Ground, MD 21010-5401